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HYPERTENSION IN PEOPLE OVER FORTY

COMMANDER A. M. MASTER, MC-V(S), U.S.N.R.

H. H. MARKS, A.B.

BETHESDA, MD.

AND

CAPTAIN SIMON DACK

MEDICAL CORPS, ARMY OF THE UNITED STATES

In a previous communication we [1] intimated that the incidence of hypertension in the general population over 40 and 50 was higher than was generally appreciated. This has been confirmed in preliminary reports [2] on the incidence of hypertension in workers over 40 and in general hospital patients. In this report we now summarize the blood pressure readings in nearly 15,000 men and women over the age of 40.

The problem of hypertension is a fundamental one. Together with coronary sclerosis it is the most common form of heart disease and probably is the largest single cause of death. This is doubly so if only those over 40 are considered. Furthermore, hypertension is important in respect to the role it plays in other diseases, e. g. arteriosclerosis of the cerebral, renal and coronary vessels.

The incidence of hypertension in persons over 40 has become increasingly important because there are now millions of people who survive this age.[3] One third of the present population is 40 years or over [4] and it has been estimated that in 1980 nearly one half will be.[5]

The literature on hypertension is voluminous. Yet reports on the incidence of hypertension in large series of people over 40 years of age have been few. In the few reports that discuss hypertension in older age groups the number of cases has been too small to be reliable, often only 100 cases.[6] Furthermore, frequently only blood pressure averages for each age group are given; but these are not helpful in determining the incidence of hypertension.

The tremendous material presented by insurance statistics cannot be used, since they consist of a selected group. People with serious degrees of hypertension either do not present themselves to the insurance companies or are rejected and therefore not included in the published figures. Nevertheless, that the blood pressure increases with age is definite.[7]

MATERIAL

We have collected blood pressure readings on 14,849 persons over 40 years of age (tables 1 and 2). There were 5,737 workers,[8] none in industries exposed to poisons; 2,610 residents of homes for aged,[9] rather than homes for aged and sick; and finally 6,502 patients in a general hospital (Mount Sinai, New York City) in which only a small percentage were admitted for hypertension or its complications. There were 8,483 men and 6,366 women. The material was divided according to sex and ten year age groups. All the groups, except that comprising the ages 90 to 99, were of sufficient size to give statistically reliable results (tables 1 and 2).

METHOD OF TAKING BLOOD PRESSURE

All the blood pressures were taken by the auscultatory method by physicians. In the industrial concerns the blood pressure readings of the women were nearly always taken by women doctors.

In nearly two thirds of the readings the diastolic pressure was taken at the fifth phase—the complete disappearance of sound rather than at the fourth phase—the definite diminution in intensity. The American

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From the Naval Medical School, National Naval Medical Center, Bethesda, Md., the Cardiographic Laboratory, Mount Sinai Hospital, New York, and the Statistical Bureau, the Metropolitan Life Insurance Company, New York.

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1. Master, A. M.; Dack, Simon, and Jaffe, H. L.: Age, Sex and Hypertension in Myocardial Infarction Due to Coronary Artery Occlusion, Arch. Int. Med. **64:** 767 (Oct.) 1939.

2. (a) Master, A. M., and Dack, Simon: Incidence of Hypertension in People of Forty Years of Age and Older, J. Mount Sinai Hosp. **8:** 1232 (March-April) 1942; (b) Hypertension in Workers Over Forty Years of Age, Indust. Med. **11:** 145 (April) 1942.

3. Stieglitz, E. J.: Aging as an Industrial Problem, J. A. M. A. **116:** 1383 (March 29) 1941. Longevity Almost Doubled in Six Decades, Statistical Bull., Metropolitan Life Ins. Company, New York **23:** 1, 1942.

4. Our Aging Population, Quart. Bull., City of New York Department of Health **9:** 53, 1941.

5. Osborn, Frederick: Significance to Medicine of Present Population Trends, Bull. New York Acad. Med. **15:** 427 (July) 1939. Dublin, L. I.: Statistical and Social Implications in the Problem of Our Aging Population, paper in "Medical Problems of Old Age" (a Symposium), Univ. Pennsylvania Bicentennial Conference, Philadelphia, University of Pennsylvania Press, 1941. Stieglitz.[3]

6. Bowes, L. M.: Blood Pressure in the Aged, J. Lab. & Clin. Med. **2:** 256 (Jan.) 1917. Thompson, R. J. C., and Todd, A. E.: Old Age and Blood Pressure Problems, Lancet **2:** 503 (Sept. 2) 1922. Wildt.[26] Richter.[29]

7. Woley, H. P.: The Normal Variation of the Systolic Blood Pressure, J. A. M. A. **55:** 121 (July 9) 1910. Norris, W. N.; Bazett, H. C., and McMillan, T. M.: Blood Pressure: Its Clinical Applications, ed. 4, Philadelphia, Lea & Febiger, 1927. Willius, F. A.: The Heart in Old Age: A Study of Seven Hundred Patients Seventy-Five Years of Age and Older, Am. J. M. Sc. **182:** 1 (July) 1931. Fisher.[12] Symonds.[32] Hunter.[33] Blood Pressure.[42] Saller.[27] Gager.[42] Wetherby.[28] Fishberg.[10] Saunders.[39] Miller.[18] Master, Dack and Jaffe.[1] Wildt.[26] Bowes.[6] Thompson and Todd.[6] Richter.[29]

8. The data on industrial workers were obtained from the New York Telephone Company, New York (Dr. E. McSweeney), from the General Motors at the Saginaw plant in Michigan (Drs. Clarence Selby and R. D. Mudd), from the E. I. du Pont de Nemours Company, Wilmington, Del. (Dr. G. H. Gehrmann), from R. H. Macy & Co., New York (Dr. Michael Lake) and from the B. Altman Company, New York (Dr. Louis Hausman).

9. The material was gathered from the City Home for Dependents, New York (Maxwell Lewis and Dr. William A. Buck), Brooklyn Hebrew Home and Hospital, New York (Dr. Herbert Schreiber), Home for Aged and Infirm Hebrews, New York (Dr. F. D. Zeman), Home for Old Men and Aged Couples (Christina Sutherland), Hebrew Home for the Aged of Harlem, New York (I. Spira), Theodore Presser Foundations, New York (James Cooke and Dr. W. A. Buck), Presbyterian Home, New York (Dr. C. F. Collins), Peabody Home, New York (Dr. T. L. Fisk), Sisters of St. John the Baptist, New York, Seabury Memorial Home, New York (Mrs. Mank), Samaritan Home, New York (Mary Lord), Braker Memorial Home, New York (W. M. Arnold), Mariner's Family Asylum for Aged Women of the Sea, New York (Nellie Oxley), and St. Teresa's Guest House, New York (Mother Mary Casen).

Heart Association [10] has recommended that the former be used. Most clinicians, however, still use the fourth. Since the blood pressure reading at that point averages at least 5 mm. higher than the fifth,[11] it is readily seen that had the former method been consistently employed the percentages of hypertension in our series would be higher.

In our preliminary reports, we [2] have already presented in detail our reasons for concluding that our cases are representative of persons in middle and later life in the general population as a whole and therefore summarize them here only briefly. Among the industrial cases over 40, every type of worker was represented: clerk, telephone operator, longshoreman, linesman, chauffeur, laborer, executive and others. The data were obtained from companies possessing a complete medical service, where the individual is examined at application for employment and often regularly thereafter at six or twelve month periods, where voluntary examinations may be had at any time, where complete records are kept and where necessary precautions are taken to obtain correct blood pressures. Thus, these blood pressure readings are dependable. Although we were assured by the medical directors that only a very high blood pressure would bar an applicant from employment, it may be that in times when jobs are scarce hypertension may be used as an excuse not to hire an applicant. On the other hand, workers were not discharged for uncomplicated hypertension. To a slight extent our figures are low, since they would not include hypertensives rejected on application for a job. As already indicated, records of employees were excluded if the workers were exposed to toxic chemicals, fumes and so on, which affect bodily health and blood pressure.

With regard to the hospital material obtained from the Mount Sinai Hospital, New York,[2a] the data were derived from all types of patients in a large institution of 1,000 beds, consisting of open wards and semiprivate and private patient pavilions. There is no unusual concentration on any specialty, and cases included are drawn from every department—medicine, surgery, neurology, gynecology, otolaryngology, ophthalmology and others. All classes of people, rich and poor, banker and laborer, are represented.

To be sure that the admissions to the hospital for hypertension, hypertensive heart disease or heart failure and cerebral apoplexy were not significantly high, three hundred charts of each decade except the ninth were sampled. If a patient was admitted for hypertension and another disease, e. g. diabetes, and there was any doubt as to the primary condition, we classified it as a hypertension admission. It is evident from table 3 that admissions for hypertensive disease or its direct complications (2.0 to 8.5 per cent) constitute an unimportant and not undue proportion of the total admissions.

As regards the homes for the aged a definite attempt was made to obtain data from institutions where the basis of admission was age rather than infirmity; that is, institutions where the resident could spend the rest of his days in security, where he usually paid something

TABLE 1.—*Hypertension in Men 40 Years of Age or Over*

Percentage with specified degree of hypertension classified according to age groups and source of material.

Degree of Hypertension,* Mm.	Source of Data	Percentage at Ages					
		40-49	50-59	60-69	70-79	80-89	90-99§
140/90 or over	All groups	33.6	49.2	66.5	77.1	77.7	87.0
	Industry	32.1	44.9	62.4	81.1	‡	....
	Homes for aged	50.0†	73.4	78.2	86.1	84.4	87.0
	Hospitals	37.1	50.6	58.4	63.6	61.3	....
150/90 or over	All groups	25.9	40.6	56.3	65.5	66.5	78.3
	Industry	23.8	34.7	49.5	62.3	‡	....
	Homes for aged	34.4†	60.4	70.1	74.8	75.0	78.3
	Hospitals	31.7	43.6	47.6	52.6	44.0	....
150/95 or over	All groups	16.9	32.8	51.0	61.8	63.3	73.9
	Industry	16.1	29.0	41.7	58.5	‡	....
	Homes for aged	34.4†	57.3	65.1	71.2	71.7	73.9
	Hospitals	18.7	33.6	43.2	48.8	42.7	....
150/100 or over	All groups	15.4	31.7	50.4	61.3	63.3	73.9
	Industry	14.8	27.6	39.8	56.6	‡	....
	Homes for aged	34.4†	57.3	64.8	70.6	71.7	73.9
	Hospitals	16.4	32.8	42.9	48.8	42.7	....
Systolic 150 or over	All groups	13.6	29.7	48.8	58.4	61.3	73.9
	Industry	13.4	26.8	39.8	56.6	‡	....
	Homes for aged	28.1†	47.6	61.2	66.1	68.9	73.9
	Hospitals	13.9	30.5	42.1	47.7	42.7	....
Diastolic 90 or over	All groups	22.7	34.2	43.7	47.3	41.8	52.2
	Industry	20.6	28.1	33.9	35.8	‡	....
	Homes for aged	28.1†	60.8	57.8	58.9	47.8	52.2
	Hospitals	28.7	36.8	36.1	32.4	26.7	....
Diastolic 95 or over	All groups	10.3	20.5	26.6	32.6	27.9	21.7
	Industry	8.9	17.1	19.7	22.6	‡	....
	Homes for aged	25.0†	39.9	36.8	42.3	32.8	21.7
	Hospitals	14.0	21.5	21.0	20.2	13.3	....
Number of cases	All groups	3,386	2,256	1,607	895	226	23
	Industry	2,492	1,124	319	53	1	..
	Homes for aged	32	143	619	496	180	23
	Hospitals	862	989	729	346	75	..

* Cases are included if either the systolic or the diastolic is within the specified limits.
† Ratio not reliable because of small number of cases.
‡ Only 1 case in study.
§ All 23 men in this age group were from homes for the aged. Ratios in this column are not reliable because of the small size of the sample.

TABLE 2.—*Hypertension in Women 40 Years of Age or Over*

Percentage with specified degree of hypertension classified according to age groups and source of material.

Degree of Hypertension,* Mm.	Source of Data	Percentage at Ages					
		40-49	50-59	60-69	70-79	80-89	90-99§
140/90 or over	All groups	39.2	64.8	77.9	81.7	84.7	81.1
	Industry	37.0	64.3	84.2	‡	....	....
	Homes for aged	68.8†	81.1	89.0	88.3	89.5	81.1
	Hospitals	40.9	62.8	72.6	72.6	65.4	....
150/90 or over	All groups	32.0	53.4	67.7	73.3	76.6	73.0
	Industry	30.2	53.6	73.7	‡	....	....
	Homes for aged	56.3†	72.5	82.1	80.8	80.9	73.0
	Hospitals	33.6	51.2	61.1	62.7	....	....
150/95 or over	All groups	23.6	46.6	64.5	70.2	74.3	70.3
	Industry	20.6	45.1	69.7	‡	....	....
	Homes for aged	43.8†	63.8	78.9	78.5	78.0	70.3
	Hospitals	26.2	44.8	57.9	58.4	59.6	....
150/100 or over	All groups	22.7	45.5	64.0	69.5	74.3	70.3
	Industry	19.7	43.5	69.7	‡	....	....
	Homes for aged	43.8†	68.0	78.6	77.5	78.0	70.3
	Hospitals	25.2	43.8	57.3	58.1	59.6	....
Systolic 150 or over	All groups	20.8	44.4	63.4	68.0	72.8	70.3
	Industry	17.7	41.9	68.4	‡	....	....
	Homes for aged	43.8†	65.1	78.0	75.3	76.1	70.3
	Hospitals	23.4	43.0	56.7	57.4	59.6	....
Diastolic 90 or over	All groups	26.6	42.7	46.0	52.0	54.8	48.6
	Industry	35.1	41.7	51.3	‡	....	....
	Homes for aged	50.0†	62.4	62.1	61.5	57.4	48.6
	Hospitals	27.7	40.8	38.6	39.9	44.2	....
Diastolic 95 or over	All groups	13.3	24.0	29.2	34.3	35.6	24.3
	Industry	11.3	21.4	28.9	‡	....	....
	Homes for aged	31.3†	44.0	40.1	44.3	37.3	24.3
	Hospitals	15.9	22.8	24.4	22.1	28.8	....
Number of cases	All groups	2,656	1,469	1,240	712	261	37
	Industry	1,279	384	76	9	....	..
	Homes for aged	16	109	346	400	209	37
	Hospitals	1,361	967	818	303	52	..

* Cases are included if either the systolic or the diastolic is within the specified limits.
† Ratio not reliable because of small number of cases.
‡ Only 9 cases in study.
§ All 37 women in this age group were from homes for the aged. Ratios in this column are not reliable because of the small size of the sample.

10. Standard Method for Taking and Recording Blood Pressure Readings, Joint Recommendations of the American Heart Association and the Cardiac Society of Great Britain and Ireland, J. A. M. A. **113**: 294 (July 22) 1930.

11. Hunter, A.: Blood Pressure: What Affects It? Proc. A. Life Insur. Pres. **17**: 64, 1923. Blood Pressure Study, 1939, Actuarial Society of America and the Association of Life Insurance Medical Directors, New York, 1940. MacKenzie and Shepherd.[12]

or contributed his entire savings for his future upkeep. Probably two thirds of the residents did this. Protestants, Catholics and Jews were represented; less than one fourth were Jews. Complete records of blood pressure were kept in all instances and competent physicians made a physical examination once or twice a year regularly.

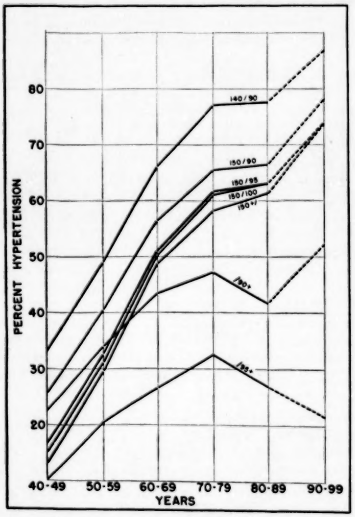

Chart 1.—Hypertension in men aged 40-99.

It is true that no one group, either workers, hospital patients or residents in the homes for the aged, is representative of the population as a whole. The incidence of hypertension was not identical for these three groups. However, since the aggregate is based on all classes of the population, it may be considered to be a fair cross section of it.

LIMITS OR DEFINITION OF HYPERTENSION

Clinicians and insurance investigators[12] have for years been interested in the limits to be used for hypertension. The definition of the latter is by no means specific. Various authors have used different lower limits of systolic and diastolic pressures, and in much of the earlier literature, and even some current literature, hypertension is defined merely in terms of the systolic. Some authors have related the lower limit to an arbitrary figure above the average for the age. In the past, a lower limit of 150/100 was in common use, but this was subjected some years ago to criticism as being too liberal, chiefly on the basis of insurance mortality studies.[13] Some authorities now set the limit of beginning hypertension as low as at 140 mm. systolic or 90 mm. diastolic. In recognition of the arbitrary nature of the classification of hypertension, we are reporting the facts on the basis of seven definitions, namely 140/90 or over, 150/90 or over, 150/95 or over, 150/100 or over (with either the systolic or diastolic pressure qualifying the case for the particular class), 150 mm. systolic or over, 90 diastolic or over and 95 diastolic or over (tables 1 and2).

RESULTS

Tables 1 and 2 give the combined results for the three broad classes of persons included in the study, subdivided according to age and sex, and these facts are presented graphically for men and for women in charts 1 and 2 respectively. Because of the relatively small number of cases over the age of 90, the changes between the ninth and tenth decades of age are indicated by broken lines.

On the basis of the customary limit of hypertension, 150 and/or 90 or over, a little over one fourth of the men have hypertension at ages 40-49, a little over two fifths in the next decade, considerably more than half in those 60-69, nearly two thirds in 70-79 and slightly more in the ninth decade. Among women the general contour of the age curve bears a general resemblance to that for males, but the proportions are much higher,

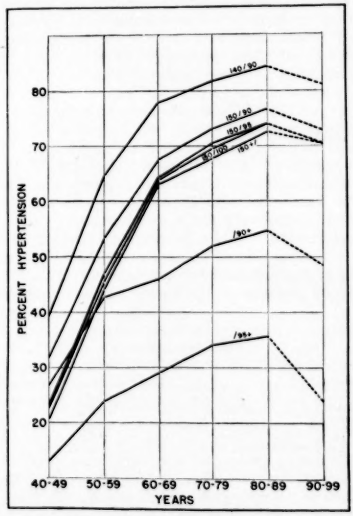

Chart 2.—Hypertension in women aged 40-99.

there being characteristic differences in the level and the steepness of the curves. In the first age group, 40-49, almost a third have hypertension, more than half

12. Fisher, J. W.: The Diagnostic Value of the Sphygmomanometer in Examinations for Life Insurane, J. A. M. A. **63:** 1752 (Nov. 14) 1914. Symonds, Brandreth: The Blood Pressure of Healthy Men and Women, ibid. **80:** 232 (Jan. 27) 1923. Gager, Leslie C.: Hypertension, Baltimore, Williams and Wilkins Company, 1930. Janeway, T. C.: A Clinical Study of Hypertensive Cardiovascular Disease, Arch. Int. Med. **12:** 755 (Dec.) 1913. Edens, E.: Die Krankheiten des Herzens und Gefässe, Berlin, Julius Springer, 1928, p. 426. Hines, E. A., Jr.: Range of Normal Blood Pressure and Subsequent Development of Hypertension: A Follow-Up of 1,522 Patients, J. A. M. A. **115:** 271 (July 27) 1940. Basic Studies of the Aging Cardiovascular System, New York, Metropolitan Life Insurance Company, 1940. Daley, R. M.; Ungerleider, H. E., and Gubner, R. S.: Prognosis and Insurability of Hypertension, with Particular Reference to the Electrocardiogram, Proc. A. Life Insur. M. Dir. America **28:** 18, 1942. Blood Pressure Study, 1939.[11]

13. MacKenzie, L. F., and Shepherd, P.: The Significance of Past Hypertension in Applicants Later Presenting Normal Average Blood Pressures, Proc. A. Life Insur. M. Dir. America **24:** 157, 1937. Blood Pressure: Association of Life Insurance Medical Directors and the Actuarial Society of America, New York, 1925. Blood Pressure Study, 1939.[11]

in the next decade, more than two thirds in the seventh decade and about three fourths in the eighth and ninth decades.

Turning to the lowest limit of hypertension, namely 140 and/or 90 or over, it is found that about one third of the men between 40 and 49 years of age have hypertension, but this proportion increases rapidly for the next three decades, until it is over three fourths in the eighth. Among women the incidence of hypertension of this degree is approximately 40 per cent between the ages 40 and 49, rising rapidly and exceeding the three quarter mark between 60 and 69. The proportions continue to increase, but more slowly, through the ninth decade, when 85 per cent of the women have a blood pressure of 140/90 or over.

A study of the charts reveals that, for all the seven limits of hypertension used, the incidence of hypertension rises with each decade until the age of 80. The curves containing systolic blood pressure limits rise, in fact, until 90. The percentage is always higher in women.

When only diastolic blood pressure is considered, there is found to be a definite lag in the upward slope of the curve of blood pressure with age, beginning at the age of 60, and in men the proportion actually falls after age 80. This emphasizes the well known observation that the systolic rises more than the diastolic with age, thus causing the pulse pressure to increase.

It is of interest to see how great the proportion of hypertensives is among persons in the general population who are past their fortieth birthday on the assumption that our findings are representative. Computations of this type, taking into account the increase in the proportion of cases with high blood pressure with advancing age, have been made on the basis of the age distribution of the white population of the country at the census [14] of 1940. These computations have been done for several broad age groups, viz. 40 and over, 50 and over, 60 and over and 70 and over, according to three of the definitions of hypertension (table 4).

By the most liberal definition of hypertension, 140/90 or over, practically half the male population and 60 per cent of the female population 40 years of age and over are hypertensive. These proportions increase rapidly so that, among persons 70 and over, more than three fourths of the men and four fifths of the women have high blood pressure of this degree. Even by the much more conservative definition of 150/100 or over about one third of the male population and over two fifths of the female population at ages 40 and over have high blood pressure. This percentage also rises rapidly, so that it is present in more than a majority of men 60 and over and of women 50 and over.

TABLE 3.—*Hospital Admissions for Hypertension or Its Complications*

Age Group	Male	Female
40-49	2.0%	3.5%
50-59	5.2%	7.7%
60-69	3.3%	5.3%
70-79	4.8%	8.5%

In New York City, where most of the fundamental material was derived, the proportions would be slightly lower. The reason for this is that the New York City population has a smaller proportion of persons at the ages past 60 than is true for the rest of the country.

The proportion of Negroes in our series is much lower than in the total population. If allowance should be made for this factor it would increase our figures somewhat, since hypertension has been reported to be appreciably more frequent in Negroes [15] than in white persons.

TABLE 4.—*Estimated Incidence of Hypertension of Various Degrees Among White Persons in the General Population Over Age 40*

Based on the incidence in the survey and the age distribution of the population of the United States in 1940.

Degree of Hypertension,* Mm.	Age Group Years	Percentage	
		Male	Female
140/90 or over	40 and over	49.8	59.8
	50 and over	59.9	72.5
	60 and over	70.5	79.6
	70 and over	77.3	82.2
150/90 or over	40 and over	40.9	50.7
	50 and over	50.3	62.2
	60 and over	59.8	70.2
	70 and over	65.8	74.0
150/100 or over	40 and over	32.5	43.6
	50 and over	43.2	56.5
	60 and over	54.7	66.5
	70 and over	61.8	70.4

* Cases are included if either the systolic or the diastolic is within the specified limits.

Since most of the persons included in the study were residents of New York City, which has a large Jewish population, it might be inferred that this was a major factor in the high incidence of hypertension reported. However, only among hospital cases were Jews in the majority—about 60 to 65 per cent. As regards homes for the aged, three fourths of the patients were non-Jewish. The proportions in the industrial cases are not known exactly, but probably less than 10 per cent were Jewish. It is significant also that practically the same ratios of hypertension were observed in the different industrial concerns we have used in our study, whether located in New York or elsewhere.[2b]

COMMENT

It is surprising that there has not been an appreciation of the prevalence of hypertension in people over 40 or 50 years of age. However, the indications of this high prevalence have been present if one searched for it, since numerous papers[16] have shown that the average blood pressure goes up with age. Although the recording of average blood pressure in an age group is no help in respect to the incidence of hypertension, the paper of Britten and Thompson [17] and also the recent one of Miller [18] show a distinct trend of increase in hypertension with age. Thus, analysis of the data of Britten and Thompson shows in 2,638 male workers an incidence of hypertension (150 mm.) of 16.0 per cent in ages 40-49, 28.6 per cent in ages 50-59 and actually 51.2 per cent in the age of 60 years or over. These authors inferred that the high incidence of hypertension at the

14. Age Composition of the Population for the United States, Urban and Rural, and for States, 1940 (Sixteenth Census of the U. S. Series P-10, No. 6), U. S. Dept. of Commerce, Bureau of Census, Washington, D. C., 1942.

15. Adams, J. M.: Some Racial Differences in Blood Pressures and Morbidity in a Group of White and Colored Workmen, Am. J. M. Sc. **184:** 342 (Sept.) 1932. Hunter,[11] Saunders and Bancroft.[6]

16. Fishberg, A. M.: Hypertension and Nephritis, ed. 4, Philadelphia, Lea & Febiger, 1939. Lewis, W. H., Jr.: Changes with Age in the Blood Pressure in Adult Men, Am. J. Physiol. **122:** 491 (May) 1938. Mosenthal, H. O.: Relation of the Kidney to Blood Pressure, New York State J. Med. **41:** 953 (May 1) 1941. Woley,[7] Fisher,[12] Symonds,[13] Hunter,[11] Norris, Bazett and McMillan,[7] Saller,[27] Gager,[12] Willius,[7] Wetherby,[28] Saunders and Bancroft,[10] Edens,[12] Wildt,[26] Bowes,[4] Thompson and Todd,[8] Richter.[29]

17. Britten, R. H., and Thompson, L. R.: A Health Study of Ten Thousand Male Industrial Workers, Pub. Health Bull. 162, U. S. Public Health Service, June 1926, p. 170.

18. Miller, Isidore: Blood Pressure Studies in the Aged, New York State J. Med. **41:** 1631 (Aug. 15) 1941.

older ages was common only to workers. As already stated, Saunders and Bancroft [19] found a 62.3 per cent incidence of hypertension (systolic 150 mm. or more) in female Negroes of ages 50-59, 73.5 per cent of ages 60-69 and 73.1 per cent over 70. These investigators explained their findings away on the basis of poverty of the people and the frequency of avitaminosis among them.

Our survey of persons over 40 shows such high proportions with hypertension of slight and moderate degree that we believe it calls for some revision of our point of view as to what is normal for persons in middle and later life. It may well be that the definition of hypertension needs to be liberalized. For clinical medicine, certainly, if at least half the persons over 50 have a blood pressure of at least 150/90 it can hardly be said that such a degree of hypertension is abnormal. This point of view does not in any way conflict with the fact that pressures below this level are more favorable for longevity. We do not say, for example, that a man 60 years old with blood pressure 160/95 will live as long as one whose blood pressure is 120/80. That cannot be predicted for the individual. The chances are better for the man with the lower blood pressure because, when groups are considered, the mortality of those with higher blood pressure is appreciably in excess of those with low blood pressure. As far as longevity is concerned, insurance studies clearly show that the hypotensive have the best outlook. Richter [20] noted the frequency of very low blood pressures in very old persons. To the extent that the expected longevity is a rough index of physical and mental well-being, Robinson [21] may be correct in saying that hypotension is ideal, but we believe that he is wrong in intimating that the blood pressures beyond 140 or 150, let alone any blood pressure over 120, are "pathologic." It may well be that these higher pressures are a general and early indication of cardiovascular degeneration. But, of themselves, such pressures cannot be looked on as pathologic. Group longevity is not the sole criterion. Experience shows that in many persons hypertension is not incompatible with a high degree of mental and physical efficiency over long periods of time.

The data of this survey permit the construction of frequency distributions of blood pressures for persons over 40 and the computation of the normal range according to various statistical criteria. The preparation of this material is under way.

That the high percentage of hypertension in the population over 40, and particularly over 50, is no cause for alarm should be evident. Rather, it should be a means of reassurance since a slight, perhaps even a moderate, degree of hypertension can no longer be considered abnormal at these ages. Fahr [22] and Wiggers [23] feel that it is compensatory to the loss of elasticity that occurs in aging blood vessel walls. Since the aorta has lost its elasticity at each systole, the blood pressure is high. This physiologic reasoning also explains the increase in pulse pressure with age,[24] for during diastole, as the blood flows off to the tissues of the body, the pressure falls rapidly since there is little elastic recall to the vessel wall. One might even hazard the opinion that the arteriosclerosis causes the hypertension and not vice versa.

We have mentioned the tendency of our curves to flatten after the age of 70, but the systolic hypertension certainly and even the diastolic (except in men from 80 to 89) rises until the age of 90. This is contrary to most series reported, which show a fall after the age of 65.[25] Wildt,[26] however, found in his small series a rise to 90. Saller's [27] data indicate a rise in blood pressure past 70 years of age. Wetherby [28] found increasing average blood pressure in older persons, but his data, based on the age group 70 and over, give no clue as to the situation in extreme old age. Undoubtedly the discrepancy is due to the fact that the number of cases in the age groups between 65 and 90 cited by previous investigators was very small, often consisting of 100 or 150 cases, including both men and women.

Concerning the absolute level of incidence of hypertension after the age of 90 we can say nothing, since the number of cases here is too small. We have used broken lines in the graphs to indicate this uncertainty.

SUMMARY

Since hypertension is most common in persons over 40 and because of the greatly increased number of people surviving this age, the incidence of hypertension at these ages is important.

The 15,000 persons in the survey (8,483 males and 6,366 females) represent a good cross section of the population in middle and later life. In each decade of life from the fifth to the ninth the size of the samples was sufficient to give statistically reliable results. The blood pressure readings were dependable.

The incidence of hypertension in each decade of life was determined according to seven limits, namely 140/90 or over, 150/90 or over, 150/95 or over, 150/100 or over, 150 mm. or over systolic, 90 or over diastolic and 95 or over diastolic.

In each decade of age a large proportion of persons were found to be hypertensive. This was true particularly of systolic hypertension. Among men a majority were hypertensive beginning with age 60 for most of the limits, and among women this occurred in some instances as early as age 50.

The percentages of hypertensive persons by decade were applied to the white population of the United States as constituted in 1940, and it was found that on this basis 41 per cent of the male population and 51 per cent of the female population 40 years of age and over would be expected to have blood pressures of 150/90 or over. At age 50 and over this ratio would be 50 per cent in males and 62 per cent in females, at age 60 and over, 60 per cent for males and 70 per cent for females, and at age 70 and over, 66 and 74 per cent respectively.

19. Saunders, G. M., and Bancroft, Huldah: Blood Pressure Studies on Negro and White Men and Women Living in the Virgin Islands of the United States, Am. Heart J. **23:** 410 (March) 1942.

20. Richter, A.: Ueber Blutdruck im hoheren Lebensalter, Deutsches Arch. f. klin. Med. **148:** 111, 1925.

21. Robinson, S. C., and Brucer, Marshall: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, Arch. Int. Med. **64:** 409 (Sept.) 1939.

22. Fahr, George; Davis, Jay; Kerkhof, Arthur; Hallock, Philip, and Giere, Ellis: Hemodynamics of Arteriosclerosis: Influence of Change of Coefficient of Volume Elasticity on Circulation, Am. J. Physiol. **101:** 376 (July) 1932.

23. Wiggers, C. J. Physical and Physiological Aspects of Arteriosclerosis and Hypertension, Ann. Int. Med. **6:** 12 (July) 1932.

24. Fisher, J. W.: Further Report of Diagnostic Value of the Systolic Blood Pressure Covering a Period from Aug. 1, 1907 to Aug. 1, 1915, Proc. A. Life Insur. M. Dir. America, 1917, p. 203. Standard Method for Taking and Recording Blood Pressure Readings.[19] Adams.[15] Robinson and Brucer.[21]

25. Riseman, J. E. F., and Weiss, Soma: The Age and Incidence of Arterial Hypertension, Am. Heart J. **5:** 172, 1930. Bowes.[6] Fisher.[24]

26. Wildt, H.: Ueber Blutdruck in Greisenalter, Zentralbl. f. Hertz- u. Gefässer. **1:** 41, 1922.

27. Saller, K. Ueber die Alters Veränderungen des Blutdrucks, Ztschr. f. d. ges. exper. Med. **58:** 683, 1928.

28. Wetherby, Macnider: A Comparison of Blood Pressure in Men and Women: A Statistical Study of 5,540 Individuals, in The Kidney in Health and Disease, edited by Hilding Berglund and Grace Medes, Philadelphia, Lea & Febiger, 1935, p. 370.

It was found that, regardless of the classification, the incidence of hypertension rose with each decade of age up through the eighth decade, and in the case of systolic hypertension up through the ninth decade. The incidence of hypertension was higher in women and rose precipitously between 40 and 60 years of age, faster than in men.

Systolic hypertension increased more rapidly than diastolic hypertension, resulting in an increase of pulse pressure with age.

The presence of hypertension at age 40 and over is so common that a mild degree and perhaps even a "moderate" degree can no longer be considered abnormal. Limits of normal blood pressure at these ages should therefore be raised. The material of the survey is being analyzed to develop such standards.

THE RELATION OF VASCULAR DISEASE TO THE HYPERTENSIVE STATE

BASED ON A STUDY OF RENAL BIOPSIES FROM ONE HUNDRED HYPERTENSIVE PATIENTS

BENJAMIN CASTLEMAN, M.D.
AND
REGINALD H. SMITHWICK, M.D.
BOSTON

The gross and microscopic appearance of the kidneys of hypertensive patients dying of renal failure or any other complication such as coronary disease, heart failure or cerebral hemorrhage has been fairly well established from postmortem studies. The almost constant finding of renal arteriolar disease in these cases has led many people to believe that increased peripheral resistance to blood flow offered by generalized arteriolar disease, especially of the kidneys, is the cause of hypertension. Moritz and Oldt's[1] comparative study of the arterioles of 100 hypertensive and 100 nonhypertensive persons showing that 97 per cent of the hypertensive and 12 per cent of the nonhypertensive persons had renal vascular disease seemed confirmatory evidence of this premise. The other school of thought is that the arteriolar disease is secondary to the hypertension, the cause of which is still unknown. The presence of severe arteriolar damage at the end stage of the disease, as seen in autopsy material, does not necessarily indicate primary arteriolar disease. Outside of experimental hypertension in animals, opportunities for study of the kidneys in the various stages of hypertension have been too few to warrant any definite conclusions.

The surgical treatment of hypertension by dorsolumbar sympathectomy has afforded us the unique opportunity to examine the kidney grossly through this operative field and to take a biopsy. It was hoped that, if enough renal biopsies taken from hypertensive patients in all stages of the disease could be studied, light could be shed on the relation of the vascular disease to hypertension. During the past two years we have collected renal biopsies from more than a hundred hypertensive patients. This report will be based on a study of the first 100 cases.

From the Departments of Pathology and Surgery, Massachusetts General Hospital.

1. Moritz, A. R., and Oldt, M. R.: Arteriolar Sclerosis in Hypertensive and Nonhypertensive Individuals, Am. J. Path. **13**: 679-728 (Sept.) 1937.

CLINICAL DATA

The 100 patients in this series ranged from 18 to 56 years of age, the average being 39. Table 1 shows their distribution by decades. There were 43 males and 57 females. Their symptoms, which included headache, fatigue and occasionally visual disturbances, had been present from one month to fifteen years, the average being approximately six years. Most of them had systolic blood pressures over 200 mm. of mercury and diastolic pressures well over 100. The average systolic pressure was 210 and the average diastolic 130. Renal function determined by the phenolsulfonphthalein test showed that 60 per cent had normal function, that 20 per cent had a moderate reduction in excretion of the dye and that 20 per cent had a decided reduction. Renal clearance observations were performed on 20 of these patients, 15 of whom showed normal function by the phenolsulfonphthalein test. Of these 15, all but 3 showed diminished inulin clearance and renal blood flow.[2]

The eyeground changes were classified into four grades: grade 1 showed various degrees of arteriolar narrowing or constriction without nicking of venous crossings; grade 2, arteriovenous compression and narrowing, caliber changes, tortuosity or wide light reflexes in the arterioles; grade 3, retinal exudates or hemorrhages in addition to the other types of arteriolar changes, and, grade 4, edema of the optic disks with measurable elevation, usually with exudate and hemorrhage and any or all of the other changes mentioned. In this series of cases there were 32 per cent of grade 1, 28 of grade 2, 26 of grade 3 and 14 of grade 4. Five cases in which there was edema of the optic disks without measurable elevation were graded 1, 2 or 3 according to other changes. They may very well, however, have been in the earliest phase of malignant hypertension and might have been placed in grade 4. From these clinical data it is apparent that all stages of the hypertensive state are represented in this group of 100 hypertensive patients. Their renal biopsies, therefore, should provide fairly well balanced material to study the relation of the renal vascular disease to hypertension.

TECHNIC

The selection of cases for sympathectomy will not be discussed here. Other significant clinical data concerning this group of cases and others as well will be reported in another communication. The operative procedure has previously been described by one of us.[3] In brief, it consists of a bilateral extensive splanchnic denervation, the great splanchnic nerves being removed from the semilunar ganglion to approximately the midthoracic level and the sympathetic trunk being resected from the ninth dorsal to the first or second lumbar ganglion inclusive. Occasionally the third lumbar ganglion is removed as well. The operation is performed in two stages, one side being done about ten days after the other. The exposure at this operation allows for accurate examination of the adrenals and kidneys, which was done in all cases. No abnormalities of the renal artery or vein were noted other than congenital variations such as aberrant vessels to the upper pole or lower pole or both. Most kidneys were found to be

2. A more detailed account of the correlation of these findings with renal biopsies (Talbott, J. H.; Castleman, Benjamin; Smithwick, R. H., and Melville, R. S.: Renal Biopsy Studies Correlated with Renal Clearance Observations in Hypertensive Patients Treated with Radical Sympathectomy) is to be published in the Journal of Clinical Investigation.

3. Smithwick, R. H.: A Technic for Splanchnic Resection for Hypertension, Surgery **7**: 1-8 (Jan.) 1940.

of normal size. In order to observe the cortical surface, the capsule was incised with a scalpel and by means of a groove director was gently reflected over an area approximately 3 cm. in diameter. The large majority of kidneys had fairly smooth surfaces; a few were slightly granular and some had definite small scars. A wedge shaped specimen 6 to 7 mm. wide and 5 mm. deep was removed with a scalpel only, forceps not being used to prevent any injury to the tissue. The specimen was immediately dropped into a bottle of Zenker's fixative. The biopsy wound was sutured with cotton or silk and covered with a small piece of adjacent fat. No complication occurred as a result of the biopsies. In 25 cases biopsies were taken from both kidneys and in every instance the microscopic appearance on the two sides was essentially the same.

MICROSCOPIC APPEARANCE OF THE RENAL BIOPSIES

Pathologists are so accustomed to the microscopic appearance of the hypertensive kidney from autopsy material with the usual postmortem changes that at the beginning of this study some of the findings due to the early fixation (a matter of seconds) seemed so conspicuous that they were at first believed to be pathologic. One of these is the strong accentuation of the basement membrane of the straight tubules, especially of the atrophic ones in the region of a small scar, best brought out by the van Gieson stain. The rapid fixation does not allow for the usual postmortem shrinkage of the epithelial cells in the convoluted tubules, so that these cells appear ballooned out and are filled with coarse granules, and almost all meet in the center, so that only a very small lumen, which is filled with granular material, is left. The glomerular capillaries in contrast seem more widely patent than in postmortem material.

The various types of renal vascular disease have been fully described in the past. One of the best papers on the subject is that by Moritz and Oldt,[3] and we have used their classification: intimal hyalinization, medial hypertrophy and degeneration and endothelial hyperplasia. Their comprehensive description and beautiful colored drawings of these various types of arteriolar sclerosis leave nothing to be added, and the reader is referred to this work for the detailed morphology. We arbitrarily divided the vessels studied into four groups: small arterioles, under 25 microns in external diameter; large arterioles, 25 to 50 microns in diameter; small arteries, 50 to 100 microns in diameter, and large arteries, over 100 microns. Since the biopsies were taken from the peripheral cortex, very few of the large arteries were available.

Most of the biopsies that showed vascular changes contained examples of all types. Except for endothelial hyperplasia, which was found only in the arteries and some of the large arterioles, the intimal and medial changes were observed in vessels of any size. Usually no one type of vascular change was found exclusively in a given biopsy. These findings are similar to those observed by Moritz and Oldt in their autopsy series. No necrotizing arteriolitis or change in the juxtaglomerular apparatus was observed.

We graded each biopsy according to the severity of its vascular disease without knowledge of any clinical data about the patient, and it was found that there were enough differences in the degree of vascular disease to classify the group into 5 grades: grades 0, 1, 2, 3 and 4. The biopsies showed that a very few patients, usually the older ones, had an occasional focal scar with vascular disease in it. These scars are seen so often in nonhypertensive patients that it was felt that they should not influence the grading of the generalized vascular condition. This policy was also employed by Moritz and Oldt.

GRADE 0 RENAL VASCULAR DISEASE

There were 7 cases in which the biopsy showed no vascular disease. The absence of vascular disease in this group was confirmed by Drs. T. B. Mallory and A. R. Moritz. Two of these patients had biopsies taken from both kidneys and they were essentially the same. There were 4 women and 3 men; they averaged 37.7 years of age and had normal renal function. One interesting feature of this group is that 3 of the patients had adrenal tumors: two cortical adenomas and one pheochromocytoma.[4] The patient with the latter tumor had no symptoms of paroxysmal hypertension. A fourth patient in this group had symptoms suggestive of a hyperactive medullary tumor, but bilateral exploration and biopsy of the adrenals were negative.

GRADE 1 RENAL VASCULAR DISEASE

There were 21 patients, 11 men and 10 women with an average age of 40, in the group with grade 1 disease. The vascular disease in this group was so slight that at a cursory examination in many instances it might well have been missed. The number of vessels involved was relatively small and much of the involvement was observed first in sections stained for elastic tissue by the van Gieson and Weigert method. All types of vascular disease were present, but it seemed that intimal hyalinization of the arterioles and arterial endothelial hyperplasia predominated. The amount and degree of vascular disease in this group was so slight that it is very unlikely that renal ischemia produced by vascular narrowing played any mechanical role in the production of the hypertension. One patient in this group had an adrenal cortical adenoma.

TABLE 1.—*Age Distribution*

Age	Patients
10-19	1
20-29	15
30-39	34
40-49	40
50-56	10
	100

GRADE 2 RENAL VASCULAR DISEASE

There were 25 patients, 17 women and 8 men averaging 41.2 years of age, whose renal biopsies were classified as grade 2. Here the vascular disease was more advanced than the minimal changes seen in grade 1 but still not severe enough to be put with the large group 3 in which vascular disease was apparent even at a cursory glance with low magnification. In grade 2 an occasional hyalinized glomerulus was seen, but by and large the vascular disease could be considered as mild. One patient in this group had an adrenal cortical adenoma.

GRADE 3 RENAL VASCULAR DISEASE

Grade 3 patients were those whose biopsies showed vascular disease usually severe in degree in every vessel. There were many more scars and hyalinized glomeruli

4. A more detailed discussion of the incidence of adrenal tumors in this series of cases will be reported separately.

in a fair proportion of this group, but others showed apparently normal widely patent capillary tufts. Medial arteriolar hypertrophy seemed to predominate in this group. There were 33 patients in this group, 22 women and 11 men; their average age was 36.8 years. Two patients in this group had an adrenal tumor—1 a cortical adenoma and the other both a pheochromocytoma on the right side and a cortical adenoma on the left. The latter patient did not have paroxysmal hypertension.

TABLE 2.—*Correlation of Renal Biopsies with Renal Function*

Renal Vessels	Cases	Renal Function		
		Normal	Moderate Reduction	Sharp Reduction
Normal	7	7	0	0
Grade 1	21	17	3	1
Grade 2	25	16	6	3
Grade 3	33	19	6	8
Grade 4	14	1	5	8
	100	60	20	20

GRADE 4 RENAL VASCULAR DISEASE

Fourteen patients, 10 men and 4 women, with an average age of 42 years, had the most severe renal vascular disease. Every vessel was involved; many glomeruli were scarred and surrounding tubules were atrophic. Except for the absence of necrotizing arteriolitis, these biopsies suggested the so-called malignant nephrosclerosis and all but 1 patient did have decreased renal function. It might be argued that these patients should not have been subjected to sympathectomy because of their imminent uremia. Although this is probably true of some of this group, others have apparently been benefited, a few in a striking fashion.

THE QUESTION OF PYELONEPHRITIS

A few of the biopsies, more from grade 4 than from the other groups of patients, showed changes consistent with chronic or healed pyelonephritis, according to the criteria of Weiss and Parker.[5] Not all of these patients gave a history of old or chronic urinary infection, while a few with a definite pyelonephritic history showed no evidence by biopsy. It was felt, however, that a definite diagnosis of pyelonephritis was not warranted from a small biopsy which did not include any medulla.

CORRELATION OF RENAL FUNCTION WITH RENAL VASCULAR CHANGES

Renal function as measured by the phenolsulfonphthalein test showed normal excretion in 60 per cent of all the cases. When divided into their biopsy grades, it is apparent from both table 2 and chart 1 that renal function is poorer the more severe the vascular disease. These results are obviously what is to be expected, however, and constitute confirmatory evidence of the accuracy of our microscopic gradings. For example, 81 per cent of patients with grade 1 renal vascular disease had normal excretion while 93 per cent of those with grade 4 disease showed impairment in renal function. There were, of course, exceptions such as 1 case of grade 1 in which there was very poor function and 1 case of grade 4 in which there was normal function. It should be emphasized that ordinary renal function tests may fail to detect early evidence of vascular disease and usually are normal or only slightly reduced when grade 3 vascular disease is present.

5. Weiss, Soma, and Parker, Frederic, Jr.: Pyelonephritis: Its Relation to Vascular Lesions and to Arterial Hypertension, Medicine **18**: 221 (Sept.) 1939.

CORRELATION OF RETINAL VESSELS WITH RENAL VASCULAR CHANGES

The four grades of retinal change were described under clinical data. In many clinics quantitative estimation of the severity of a patient's hypertension is based wholly on the eyeground changes, and for that reason it is interesting to correlate these changes with those in the kidney. Table 3 shows that there does seem to be some correlation between these two vascular systems in the normal, grade 1 and grade 2 renal groups: 5 out of 7 of the normal renal biopsy group showed only grade 1 retinal changes, 81 per cent of the grade 1 renal showed grade 1 or 2 retinal changes. However, even in these groups there were many exceptions. With respect to the grade 3 renal group, all grades of retinal changes were about equally represented. In the grade 4 biopsy group 8 out of the 14 showed severe retinal changes.

THE QUESTION OF MALIGNANT VASCULAR NEPHRITIS AND MALIGNANT HYPERTENSION

In this series of 100 patients there were 14 who clinically fell into the class usually called malignant hypertension. All but 3 of these patients showed either grade 3 or grade 4 renal vascular disease. Nine had impaired renal function as measured by the phenolsulfonphthalein test, but none had nonprotein nitrogen retention. All of them showed grade 4 retinal changes, i. e. measurable edema of the optic disks in addition to other retinal vascular disturbances. Microscopically the diagnosis of malignant vascular nephritis is usually associated with necrotizing arteriolitis. In none of these 14 cases of so-called malignant hypertension nor in any of the remaining cases in the series was there any arteriolar necrosis. Our data thus substantiate Goldblatt's[6] experimental evidence that both hypertention and severe renal insufficiency with uremia are necessary factors in producing necrotizing arteriolitis. He was able to produce these lesions in dogs by decreasing the blood supply of both kidneys below the level that was usually necessary to cause merely benign hypertension. These 14 patients were operated on before the onset of uremia, and their kidneys, therefore, would not be likely to show any arteriolitis. Only 1 died postoperatively. Although it is not within the scope of this paper to discuss the value of sympathectomy, it is interesting to note that the 2 patients in this group who have been followed for over a year after sympathectomy now have blood pressures of 120/90 and 140/100. Their respective blood pressures before operation were 175/135 and 230/160.

TABLE 3.—*Correlation of Renal Biopsies with Retinal Vessel Changes*

Renal Vessels	Cases	Retinal Vessels			
		1	2	3	4
Normal	7	5	0	2	0
Grade 1	21	9	8	2	2
Grade 2	25	4	10	9	2
Grade 3	33	8	7	10	8
Grade 4	14	2	4	6	2
	100	28	29	29	14

6. Goldblatt, Harry: Studies on Experimental Hypertension: VII. The Production of the Malignant Phase of Hypertension, J. Exper. Med. **67**: 809-826 (May) 1938.

FOLLOW-UP

Obviously great care is being taken to follow these patients. Our follow-up data at the present time in the individual renal biopsy groups are inadequate for us to attempt to predict which cases will respond to sympathectomy. However, it is of interest to report

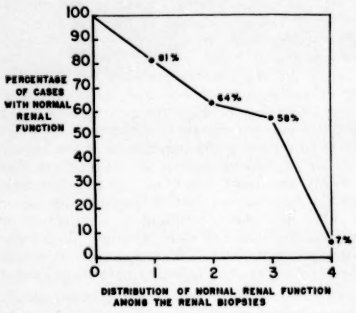

Chart 1.—Distribution of normal renal function among the renal biopsies.

that to date data are available on 21 patients who have been followed for at least a year. Most of these are in grades 2 and 3 renal vascular disease and have responded well. For example, the 7 patients in grade 2 that have been followed for a year have all had a fall in blood pressure averaging 45 mm. of mercury systolic and 20 mm. diastolic. Ten out of 11 patients in grade 3 had falls in pressure averaging 70 mm. systolic and 35 mm. diastolic. Only 1 patient with grade 4 renal disease has been followed for a year. He is back at work and his pressure, which was 212/144 preoperatively, is now 160/100. The blood pressures of 2 patients with grade 1 renal disease have not changed appreciably. We have just recently had the opportunity of studying a second biopsy taken one year after the first from a woman aged 27, and although her blood pressure, which was 235/145 before splanchnic resection, is now 150/100, the renal disease, which was classified as grade 3, has not changed.

COMMENT

The most striking result of this work is the finding of such a high percentage of renal biopsies in which there is no or only minimal vascular disease. Seven per cent were graded 0, 21 per cent grade 1 and 25 per cent grade 2; i. e., 28 per cent and possibly 53 per cent of the cases showed renal vascular systems so slightly damaged that it seems unlikely that the blood flow could have been embarrassed sufficiently to be the one factor responsible for the hypertension. A valid objection might be raised that a biopsy as small as the ones removed in this series is not an adequate sample of the whole kidney. We believe, however, that since great care was taken to select a representative region for biopsy and since similar morphologic findings were present in both kidneys in those 25 cases in which bilateral biopsies were taken, each biopsy is a fair sample of the renal tissue in the respective case. When the preliminary report of this work was presented before the American Association of Pathologists and Bacteriologists in April 1941,[7] biopsies on only the first 16 cases were available. The statement was made then that all of the specimens showed definite and fairly severe vascular disease. In view of additional evidence, it is apparent that this series was too small and included a high proportion of cases in which there was more severe hypertension. The biopsy grades of these 16 cases were 3 in grade 4, 11 in grade 3 and 2 in grade 2. It was our feeling at that time that since nearly all the biopsies showed moderate to severe vascular disease with relatively little if any renal impairment, perhaps the anatomic changes had probably antedated the hypertension. In the larger series of 100 patients, however, there were 53 who had normal kidneys or minimal renal vascular disease. Most of these patients, however, had had their hypertension for years, and almost 30 per cent of them had hypertension which was clinically severe, some associated with cerebral hemorrhage or thrombosis.

The following is a case in point:

A housewife aged 38 developed mild hypertension, 150/90, during the second trimester of her first pregnancy sixteen years before admission. Her blood pressure returned to normal following this pregnancy but rose again during her second pregnancy three years later. Ever since then she had had mild hypertension and during the past five years complained of fatigue, palpitation, dyspnea on exertion and occasional headaches. Examination four years before entry showed normal ocular fundi except for slight arterial constriction, grade 1. The blood pressure was 170/110. There was no albuminuria. The heart was not enlarged. Two years later slight cardiac enlargement was demonstrable, and there was a faint trace of albumin in the urine. Finally during the year before admission severe occipital headaches, increasing fatigue and nervousness developed. Her blood pressure was 260/150, the heart was large and the fundi showed 1 to 2 diopters of papilledema. The urea clearance was 92 per cent of normal.

Here, then, is a patient who had mild hypertension for many years and then suddenly so-called malignant

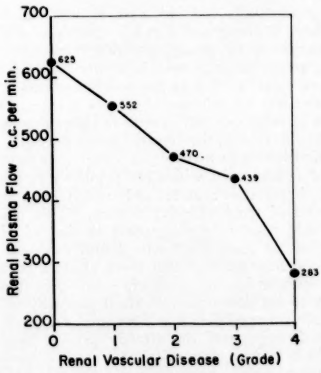

Chart 2.—Average renal plasma flow values for each of the five grades of renal vascular disease.

hypertension developed. Her renal biopsy showed only grade 1 changes—changes with luminal arteriolar narrowing so slight that under no circumstances could they alone be held responsible for the origin of the hyper-

7. Castleman, Benjamin; Smithwick, R. H., and Palmer, R. S.: Renal Biopsies from Hypertensive Patients, abstr. from Scientific Proceedings of the 41st annual meeting of the American Association of Pathologists and Bacteriologists, Am. J. Path. **17**: 617-619 (Dec.) 1941.

tension. It seems reasonable to infer, therefore, that her hypertension antedated her renal vascular disease. It is very probable that a renal biopsy performed a few years before would not have shown any vascular change.

This patient is one of the group of 21 (grade 1) having such minimal evidence of renal vascular disease that one is led to believe that the hypertensive state antedated the vascular disease. This possibility seems even more likely when one considers that 7 cases in this series, some with severe long-standing hypertension, had no renal vascular disease at all (grade 0). It can further be stated that, in many of the 25 cases presenting grade 2 renal vascular disease in which the changes did not appear severe enough to have diminished the vascular bed to cause hypertension, the hypertension may also have antedated the vascular disease. This is in keeping with Cox and Dock's [8] recent perfusion experiments on kidneys post mortem in which they found that "most kidneys from patients with hypertension without uremia have vascular beds in the normal range." In another paper,[2] based on 20 of the cases reported here, it has been shown that a correlation appears to exist between renal vascular disease and renal plasma flow. Chart 2 shows the average renal plasma flow values for each of the five grades of renal vascular disease. It is interesting to note that in the grade 0 and grade 1 renal

TABLE 4.—*Distribution of Peripheral Vascular Disease Found in Renal Biopsies*

Renal Vessels	Cases	Peripheral Vascular Disease	
		Present	Absent
Normal	3	0	3
Grade 1	14	1	13
Grade 2	12	6	6
Grade 3	11	6	5
Grade 4	6	4	2
	46	17	29

biopsy groups there was very little if any reduction in blood flow; in the grade 2 group there was a 25 per cent reduction, in the grade 3 group a 30 per cent reduction and in the grade 4 cases a 60 per cent reduction.

We are therefore led to the conclusion that a state of hypertension not infrequently exists in man in which evidence of renal vascular disease is either absent or is insufficient to explain the elevated blood pressure. The implication is that in many cases some other functional factor or factors exist which are primarily responsible for the hypertensive state and which precede the appearance of renal vascular disease. This point of view would appear to correspond to that of Homer Smith and his associates,[9] who found evidence from renal blood flow studies "that there exists a perturbation of vascular function which is primary in time and causality to the destruction of renal parenchyma." It is certainly very probable that the vascular disease, once established, aggravates the already present hypertension, which in turn accelerates the arteriosclerosis—a vicious circle. This is the stage in which the kidney is found post mortem and on which the theory of the primary vascular origin of essential hypertension is based. Our observations of the kidney biopsies in the earlier stages of hypertension have given us the missing link to help substantiate the theory that the hypertensive state precedes the renal vascular disease in many cases.

8. Cox, A. J., and Dock, William: The Capacity of the Renal Vascular Bed in Hypertension, J. Exper. Med. **74**: 167-175 (Sept.) 1941.
9. Smith, H. W.: Physiology of the Kidney, Department of Journalism Press, University of Kansas, Lawrence, 1939.

Because of the fact that renal vascular disease of consequence is known to exist in some normotensive patients dying of various causes (12 per cent in Moritz and Oldt's series) it seems probable that renal vascular disease could have been present before the onset of hypertension in some cases. In other cases renal vascular disease may result from lesions of one or both kidneys, such as pyelonephritis. Even so, the conclusion that renal vascular disease is the sole cause of hypertension under these circumstances is open to question. Granting that renal vascular disease may be present before the onset of hypertension, our data suggest that in many cases of so-called essential hypertension the elevation of blood pressure precedes the development of vascular disease in the kidney. It is not our purpose to minimize the importance of the kidney as a factor in the hypertensive state. We believe that it is probably the most important of all splanchnic viscera once it becomes involved by vascular disease or by some other mechanism resulting in a reduction or modification of the nature of its blood flow. We simply wish to indicate that the following sequence of events not infrequently exists: (*a*) hypertension and (*b*) renal vascular disease.

Just when peripheral vascular disease enters this sequence has not yet been established. There has been so much difference of opinion in the literature as to whether peripheral arterioles are or are not diseased in cases of hypertension that a study of the arterioles in biopsies of the sacrospinalis muscle in relation to the renal biopsies has been begun. At the present time we have examined only one section of muscle from 46 of the 100 cases in this series and without resorting to micrometer measurements noted that medial hypertrophy was present in only 40 per cent of the cases. Table 4 shows the distribution of these changes in the renal biopsy groups.

It is interesting to note the rare presence (7 per cent) of peripheral arteriolar sclerosis in grade 1 renal disease and the apparent increase of peripheral vascular disease in the higher renal groups (60 per cent in grades 3 and 4). Since each section contained relatively few vessels and since peripheral arteriolar sclerosis may be segmental (Moritz and Oldt [1]), it is quite possible that vascular disease may have been missed in some of the cases. Without serial sections of the blocks of tissue and perhaps micrometer measurements of the vessels, no definite conclusions should be made from these findings. If these preliminary observations are confirmed, it will be possible to conclude that the peripheral vascular disease develops after the renal disease.

SUMMARY AND CONCLUSIONS

1. Renal biopsies from 100 hypertensive patients in the course of splanchnic resections for hypertension were examined microscopically, and the degree of their vascular disease divided into five grades, as follows: grade 0, 7 per cent; grade 1, 21 per cent; grade 2, 25 per cent; grade 3, 33 per cent, and grade 4, 14 per cent.

2. The patients averaged 39 years of age and were suffering from hypertension (average 210/130) for about six years. Sixty per cent had normal renal function as measured by the phenolsulfonphthalein test, and all showed retinal vascular changes from mere arteriolar narrowing to edema with elevation of the optic disks.

3. In contrast to the almost invariable finding of well developed arteriolar disease in the kidneys of hypertensive patients observed post mortem, 28 per cent of the biopsies showed no or insignificant vascular disease and an additional 25 per cent only mild changes.

4. From these observations it is concluded that the morphologic evidence of renal vascular disease in more than half of the cases was inadequate to be the sole

factor in producing the hypertension and that in many of these and probably others the hypertensive state antedated the renal vascular lesion, which, once established, probably aggravated the hypertension. Furthermore, these observations are not in keeping with the concept that renal ischemia due to preexisting renal vascular disease is the cause of essential hypertension in man.

5. It is of interest to note that eight adrenal tumors were found in 7 patients. Six were cortical adenomas and two were pheochromocytomas. The latter had not provoked paroxysmal attacks of hypertension.

THE ADMINISTRATION OF EGG WHITE AND AVIDIN CONCENTRATES TO PATIENTS WITH CANCER

C. P. RHOADS, M.D.
AND
JULES C. ABELS, M.D.
NEW YORK

A rational basis for the treatment of cancer is to deprive the neoplastic tissue of the components required for its growth. This basis presumes that neoplastic cells either contain certain constituents lacked by their normal analogues or that the requirement for those constituents by the cancer tissue is greater than that of normal tissue.

Recently, several types of carcinoma were reported to contain abnormally high concentrations of biotin.[1] About the same time it was noted that the addition of biotin to diets which prevented in rats the development of hepatomas induced by the feeding of butter yellow broke down the protection those diets otherwise afforded.[2] These observations do not necessarily imply that biotin is required for the induction or growth of neoplastic tissue. They do suggest the possibility however that, if biotin should be withheld from patients bearing cancer, the growth of the neoplasm might be decreased to a greater extent than would that of the normal tissues.

The existence in egg white of a protein, avidin,[3] which forms a complex with biotin has been known for several years. The oral administration of large amounts of dried egg white to rats induces in them a deficiency syndrome, presumably because the avidin prevents the absorption of dietary biotin from the gastrointestinal tract.[4] The production of a biotin deficiency in man also has been claimed. Clinical evidence of this deficiency was obtained within four to twelve weeks in normal individuals maintained on low biotin diets supplemented with about 1,000 units of avidin in the form of crude egg white. At the same time as clinical changes appeared, the urine of the subjects possessed abnormally small amounts of biotin activity.[5]

Obviously, the next step was to induce by the administration of egg white a biotin deficiency in patients with cancer and thereby to deprive the neoplastic tissue of a component possibly required in greater amounts by the tumor cells than by the normal cells. Accordingly, 2 patients with widespread cancer were given diets low in their content of biotin and supplemented with amounts of avidin several times greater than that necessary to bind in vitro the dietary biotin. The results obtained form the subject of the present communication.

CLINICAL MATERIAL

The first of the 2 patients studied was L. W., a woman aged 58 with a mammary carcinoma of grade 2. A mass in her right breast first was noted ten years before admission to the hospital. The existence of the mass had been neglected and it had been allowed to grow until the whole breast was replaced by an ulcerating tumor. This extended through the chest wall on to the right pleura with metastases to the liver and to the right axillary and supraclavicular nodes. X-ray examination failed to reveal intrapulmonary or bone metastases but did demonstrate the existence of a moderate right pleural effusion. Accordingly the patient was considered to be unsuitable for surgery or radiation therapy.

The second patient, H. M., a man aged 48 with chronic lymphatic leukemia, for four months had noticed a gradual, progressive weakness, pallor, anorexia, generalized lymphadenopathy and abdominal distention. On admission he was found to have decidedly enlarged lymph nodes in all areas; the liver edge extended to the level of the umbilicus and to the midline; the spleen extended 2 inches below the umbilicus and also to the midline. There was a moderate degree of ascites, peripheral edema, dilated abdominal veins and bone tenderness. His red cell count was 2.03, hemoglobin 35 per cent and white cells 420,000, of which 98 per cent were adult lymphocytes. A sternal marrow aspiration confirmed the diagnosis of chronic lymphatic leukemia.

Throughout the present study, neither patient received any x-radiation therapy.

METHODS

The method used for the assay of avidin [3] in the egg white and of biotin [6] in the diet and in the urine of the patients was essentially that of Snell and others.[7] The following modifications were employed:

(*a*) The Fleischmann foil yeast cake was used. Under the experimental conditions employed, the effects of biotin on the growth rate of this organism were the same as on the yeast used by Snell and his collaborators.

(*b*) To prepare a urine for its determination of biotin, a 5 cc. sample was made acid with 12 normal sulfuric acid and autoclaved at 15 pounds pressure for one hour. The p_H of the autoclaved urine was adjusted to 4.2 by the addition first of potassium hydroxide 1:1 and then of potassium hydroxide N/1. A glass electrode was employed for the titration. The urine specimen then was diluted with water to from 200 to 500 volumes and 0.25, 0.5, 1.0 and 2.0 volume samples used for assay.

(*c*) To assay the biotin content of the diet, amounts of all the foods equal to those ingested in the course of a day (other than egg white) were combined in a

Dr. Abels is Finney-Howell fellow.

From the Memorial Hospital for the Treatment of Cancer and Allied Diseases.

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1. West, P. M., and Woglom, W. H.: The Biotin Content of Tumors and Other Tissues, Science **93:** 525-527 (May 30) 1941.

2. du Vigneaud, Vincent; Spangler, Juliet M.; Burk, Dean; Kensler, C. J.; Sugiura, Kanematsu, and Rhoads, C. P.: The Procarcinogenic Effect of Biotin in Butter Yellow Tumor Formation, Science **95:** 174-176 (Feb. 13) 1942.

3. Eakin, R. E.; Snell, E. E., and Williams, R. J.: A Constituent of Egg White Capable of Inactivating Biotin in Vitro, J. Biol. Chem. **140:** 535-543 (Aug.) 1941.

4. György, Paul; Rose, C. S.; Eakin, R. E.; Snell, E. E., and Williams, R. J.: Egg White Injury as the Results of Nonabsorption or Inactivation of Biotin, Science **93:** 477-478 (May 16) 1941.

5. Sydenstricker, V. P.; Singal, S. A.; Briggs, A. P.; De Vaughn, N. M., and Isbell, H. S.: Preliminary Observations on "Egg White Injury" in Men and Its Cure with a Biotin Concentrate, Science **95:** 176-177 (Feb. 13) 1942.

6. Throughout this communication the term "biotin" is used to indicate the yeast growth effect in the assayed materials in terms of biotin equivalents.

7. Snell, E. E.; Eakin, R. E., and Williams, R. J.: A Quantitative Test for Biotin and Observations Regarding its Occurrence and Properties, J. Am. Chem. Soc. **62:** 175-178 (Sept.) 1940.

5 liter jar. Water was added to make 1 liter, and the whole was thoroughly mixed for two hours by an electric stirrer. Three aliquots (5 cc.) of this mixture then were removed for analysis. Each sample was acidified with 9 volumes of 6 normal hydrochloric acid and autoclaved at 15 pounds for one hour, the p_H of the

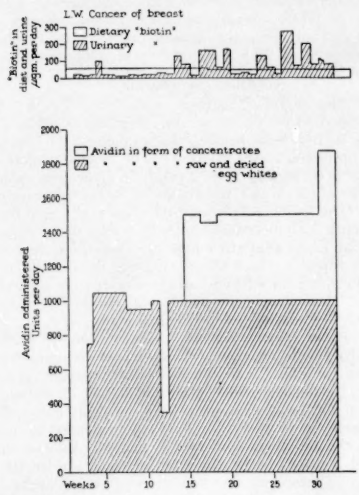
L.W. Cancer of breast
"Biotin" in diet and urine µgm. per day
Dietary "biotin"
Urinary "
Avidin in form of concentrates
" " " " raw and dried egg whites
Avidin administered Units per day
Weeks 5 10 15 20 25 30

Chart 1.—The ingestion of biotin and avidin and the urinary excretion of biotin active material by a patient with cancer of the breast.

autoclaved mixture was adjusted to 4.2 as previously described and the specimen diluted to 500 cc. Again 0.25, 0.5, 1.0 and 2.0 cc. samples were used for analysis.

Both of the patients were maintained on dietary regimens designed to induce, if possible, a biotin deficiency. When first admitted, each was given a diet which consisted each day of milk 1,150 cc., white bread 80 Gm., washed butter 30 Gm., farina 200 Gm., sucrose 50 Gm., saltine crackers 40 Gm. and lean beef 60 Gm. By analysis this diet was found to contain 60 micrograms of biotin. Supplements of 5,000 units of vitamin A, 10 mg. of thiamine, 200 mg. of ascorbic acid, 500 units of vitamin D, 6.25 mg. of calcium pantothenate, 6.25 mg. of pyridoxine and 180 mg. of ferrous sulfate were added. This diet was given to patient 1 for two weeks without the addition of avidin, during which time her urinary biotin excretion ranged from 24 to 36 micrograms and averaged 27 micrograms a day.

After a two weeks basal period in case 1 and immediately in case 2, from 1,000 to 1,200 units of avidin was added daily to their diets. The avidin was supplied in the form of about 375 Gm. of raw, frozen egg white and 165 Gm. of dried egg white. The avidin content of this raw material was found here to be 0.5 unit per gram, and that of the dried egg white from 4.0 to 5.0 units per gram. The egg white fractions either were mixed with milk or else whipped and spread on soda crackers.

RESULTS

The administration of the avidin supplements to both patients was continued for thirty weeks. In the first twelve weeks of that period the amounts of biotin excreted daily in the urine of patient 1 ranged from 6 to 132 micrograms and averaged 37 micrograms (chart 1). Thus it would appear that the addition of about sixteen times the amount of avidin to bind in vitro the biotin in the diet of this patient with mammary cancer did not decrease the urinary biotin excretion. The urine of patient 2, the man with leukemia, was not collected during this period.

The clinical condition of neither patient during the first twelve weeks of avidin ingestion was altered significantly from that expected. The ulcerated breast carcinoma of patient 1 had extended, she lost weight and bone metastases had occurred. The patient with leukemia became progressively anemic and required several transfusions. His white cell count fluctuated between 200,000 and 700,000, of which from 98 to 100 per cent were adult lymphocytes. No decrease in the size of his lymph nodes, liver or spleen were noted, but the ascites and peripheral edema did subside. However, this decrease of extravascular fluid probably was due to bed rest and a restricted fluid intake (1,500 cc. a day). In neither patient did any of the signs and symptoms attributed to a biotin deficiency [5] appear, namely desquamative macular dermatitis, ashy gray pallor, papillary atrophy of the tongue, mental changes, hyperesthesias, paresthesias, anorexia or nausea.

At the end of the twelfth week of egg white supplements the administration of avidin to both patients was increased by the addition of from 500 to 750 units of

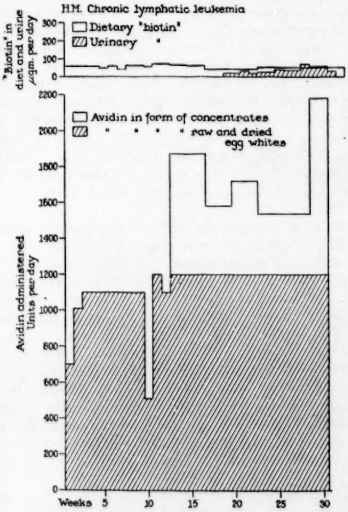
H.M. Chronic lymphatic leukemia
"Biotin" in diet and urine µgm. per day
Dietary "biotin"
Urinary "
Avidin in form of concentrates
" " " " raw and dried egg whites
Avidin administered Units per day
Weeks 5 10 15 20 25 30

Chart 2.—The ingestion of biotin and avidin and the urinary excretion of biotin active material by a patient with chronic lymphatic leukemia.

concentrated material [8] during the next sixteen weeks and by 1,000 to 1,250 units for the last two weeks of the experiment.

At this time the original diet was replaced by more palatable foods. The composition of the revised diet

8. Prepared and supplied through the courtesy of Dr. Vincent du Vigneaud and Mr. K. Dittmer, Cornell Medical College, New York City, who gave counsel and many helpful suggestions throughout the course of this investigation.

(described in the table) by analysis was found to contain 46 micrograms of biotin. The vitamin and iron supplements were continued throughout the remaining eighteen weeks of the experiment. In that period neither patient manifested any evidence of biotin deficiency. Moreover in neither instance was a decreased urinary excretion of biotin noted. Patient 1 excreted from 15 to 270 micrograms a day (average 95 micrograms a day) during the last eighteen weeks of avidin administration (chart 1). Likewise patient 2 excreted from 21 to 70 micrograms (average 38 micrograms a day) during his last thirteen weeks of avidin intake (chart 2).

Thirty weeks after the avidin therapy was first instituted the experiment was discontinued. The patient with cancer of the breast had developed intrapulmonary metastases, considerable pleural effusion and increased hepatomegaly. She finally died four weeks after the experiment was completed. The patient with lymphatic leukemia still had pronounced hepatosplenomegaly, lymphadenopathy, anemia and leukocytosis. He was treated finally by x-radiation, which induced a considerable decrease in his white cell count and lymphadenopathy.

COMMENT

The administration of from sixteen to forty times the amounts of avidin necessary to bind in vitro the biotin ingested by the 2 patients studied apparently had no effect on the course of their neoplastic disorders. Neither subject developed the clinical syndrome attributed to a lack of biotin or excreted less of that vitamin in the urine than before avidin was administered. Accordingly, these observations would suggest that the measures used were inadequate to induce the biotin deficiency syndrome described in animals and in normal human beings. Either the ratio of ingested avidin to biotin necessary to establish a clinical biotin deficiency or to decrease the urinary excretion of biotin is considerably greater than that used in the present investigation, or the avidin-biotin complex was broken down during the process of digestion so that a biotin deficiency could not be produced. In any event, to be satisfied that the administration of avidin had no effect in the growth of the cancer it would be necessary to establish in patients with malignant neoplasms clinical and experimental evidence for the existence of a biotin deficient state.

It is to be noted that patient 1 excreted more biotin in her urine than she received in her diet despite the simultaneous ingestion of large amounts of avidin. This anomalous situation likewise was observed by Oppel [9] in certain normal individuals who received amounts of egg white sufficient to bind their dietary biotin. On the other hand, the possibility exists that the biotin of the egg white and avidin concentrates administered in the present investigation were liberated by the enzymes of the foods in the diet or in the gastrointestinal tract.

In studies from this laboratory it was found that the growth of spontaneous mammary carcinoma in eight strains of mice was not affected when a typical biotin deficiency was induced in them. Also the growth of sarcoma 180 was not influenced by this dietary regimen.[10] Moreover, the inoculation of fragments of sarcoma 37 or sarcoma 180 into mice already in a biotin deficient state was followed by a tumor growth at the expected rapid rate.[11] These observations accordingly indicate that, at least in mice, no relation could be established between the existence of biotin deficiency and tumor growth.

The failure to alter the course of the neoplastic disorders in the patients studied does not mean necessarily that the oral administration of egg white and avidin will prove to be valueless in the treatment of patients with cancer. The present investigation included only 2 persons, each with a different neoplastic disorder. The effects of similar treatment of other patients with these or other forms of cancer are unknown. Moreover, the long continued administration of large amounts of egg white and avidin concentrates to subjects on a constant diet apparently does not decrease their urinary excretion of biotin, and evidently the mere feeding of large avidin supplements is not sufficient to produce clinical or experimental evidence of biotin deficiency in man.

Diet Given to the Two Patients After the First Twelve Weeks of the Experiment

		Gm.
Breakfast:	Grapefruit sections	100
	Farina	40
	Milk	160
	White bread	60
	Washed butter	20
	Sugar	15
	Jelly	30
	Coffee	200
Dinner:	Spinach	160
	Kernel corn	50
	Lean steak	110
	White bread	60
	Washed butter	25
	Canned pears	100
	Buttermilk	175
Supper:	String beans	100
	Potato	150
	Lettuce	10
	Orange sections	150
	Cottage cheese	28
	White bread	60
	Washed butter	20
	Canned pineapple	150
	Buttermilk	170

CONCLUSIONS

1. One patient bearing mammary cancer and 1 with lymphatic leukemia were fed for thirty weeks from sixteen to forty times the amounts of avidin necessary to bind in vitro the limited amounts of biotin in their diets.

2. No clinical evidence of biotin deficiency was induced in these subjects nor were the amounts of biotin excreted in their urine abnormally low.

3. No effect was noted on the expected clinical course of these patients.

York Avenue at Sixty-Eighth Street.

9. Oppel, T. W.: Studies of Biotin Metabolism in Man, Am. J. M. Sc. **204**: 856-875 (Dec.) 1942.

10. Kensler, C. J.; Rhoads, C. P., and du Vigneaud, Vincent: The Influence of Egg White and Avidin Feeding on Tumor Growth, to be published.

11. West, P. M., and Woglom, W. A.: Abnormalities in the Distribution of Biotin in Certain Tumors and Embryo Tissue, Cancer Research **2**: 324-331 (May) 1942.

Potatoes and Potassium.—Among various foods the potato has the highest potassium content, 5.5 Gm. of potassium in 2 pounds of potatoes. Potassium is a dangerous poison when injected directly into the blood and, considered objectively, potatoes are more poisonous than wine or coffee. If the potassium contained in an ordinary portion of potatoes was injected into the blood stream it could kill a man. But it never reaches the blood. A large part remains with the cellulose in the intestine and leaves the body in an indigested state. The assimilated potassium is stored in the liver and released into the blood only in the same minimal quantities in which it is excreted by the kidneys at the other end of the circulation.—Kahn, Fritz: Man in Structure and Function, volume 2, translated from the German and edited by George Rosen, M.D., New York, Alfred A. Knopf, 1943.

LEPROSY

THE CORRELATION OF ITS CLINICAL, PATHOLOGIC, IMMUNOLOGIC AND BACTERIOLOGIC ASPECTS

V. PARDO-CASTELLO, M.D.
AND
FRANCISCO R. TIANT, M.D.
HAVANA, CUBA

Leprosy affects the skin, the peripheral nervous system and the mucous membrane of the nose by preference, but other tissues and organs are also affected, often early in the disease, such as the testicles, the mammary glands, the lymphatic glands, the larynx and the eyes. Late manifestations of the liver, spleen and other internal organs may occur.

Lesions of the muscles, bones, skin, hair, nails and mucous membranes may not be directly due to the presence of Mycobacterium leprae but to trophic disturbances caused by nerve involvement.

The Correlation of the Pathology, Immunology and Bacteriology of Leprosy

	Pathology		Immunology Lepromin Test	Bacteriology
Leprosy of the skin	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary	Positive	Rare bacilli
		Sarcoidal	Positive	Rare bacilli
		Lazarine	Positive	Abundant bacilli in necrotic areas; rare in tissues
	Nonspecific	Erythematous	Pos. or Neg. 50%	Few bacilli
		Pigmented	Pos. or Neg. 50%	Few bacilli
		Achromic	Pos. or Neg. 50%	Few bacilli
Leprosy of the nerves	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary, Colliquative	Positive	Rare bacilli
	Nonspecific		Pos. or Neg. 50%	Few bacilli
Leprosy of other tissues and organs	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary, Sarcoidal	Positive	Rare bacilli
	Nonspecific ?		?	?

The preference of leprosy for the skin and peripheral nerves led to the classic conception of "cutaneous," "neural" and "mixed" types of leprosy. However, it is evident that the great majority of patients with leprosy present symptoms and signs of cutaneous, neural and visceral involvement and therefore most cases of leprosy would fall under the heading of "mixed leprosy."

On the other hand, the fact that the clinical manifestations of leprosy affect the skin, the peripheral nervous system and many other tissues and organs does not offer a definite foundation for the classification of the types of leprosy, especially as to their prognosis, epidemiology, pathology and immunology. Cutaneous lesions may be severe and of bad prognosis or may be slight and of good prognosis. Nerve involvement may be slight and chronic without much loss of function or may be severe, leading to rapid wasting and complete disability.

The leprosy congresses of Manila [1] in 1931 and of Cairo [2] in 1938 considered the classification of the clinical forms of leprosy, adhering to the old ideas and preserving the cutaneous, neural and mixed types. However, the South American dermatologists insist on the advisability of using a pathologic foundation for the classification of leprosy, following the suggestion made as early as 1936 by Eduardo Rabello Jr.[3] of Rio de Janeiro. This classification has been adopted by the South American dermatologists, among whom the contributions of the Rabellos,[4] Schujman,[5] N. V. Greco,[6] Souza Lima,[7] Moura Costa,[8] Aguiar Pupo [9] and Baliña and Bassombrio,[10] are prominent.

The pathologic changes found in leprosy are sufficiently definite and characteristic, corresponding with clearcut clinical aspects in the great majority of cases and with definite immunologic reactions and bacteriologic findings, making the correlation of these factors most important from the points of view of the prognosis and the sanitary control of the disease.

Whether leprosy affects the skin, the nervous system or the other tissues and organs, the pathologic changes may be grouped in three categories: lepromatous, tuberculoid and simple inflammatory, which we shall call nonspecific. To the trained eye these pathologic changes have clinical equivalents: the lepromatous, represented by the nodular infiltrative lesions, the tuberculoid, represented by flat infiltrated annular or ringlike, small nodular lesions and the nonspecific, represented by the macular manifestations of the skin and the simple dystrophic neural manifestations.

The fact that lepromatous lesions are extremely rich in Hansen bacilli, while the tuberculoid and nonspecific are paucibacillary and that the immunologic lepromin tests are negative in lepromatous and positive in tuberculoid types, adds strength to the practical importance of this classification.

The lepromatous and tuberculoid types are therefore definite clinical, pathologic, bacteriologic and immunologic forms of leprosy. The nonspecific types represent transitional stages and these cases may remain nonspecific for a long time or may develop into lepromatous cases or into tuberculoid cases. The tissues show only perivascular inflammation with lymphocytic infiltration. In some cases a few bacilli are scattered in the tissues or are demonstrable in the lymph and mucous membranes, while in others few or rare bacilli are found. In 40 to 60 per cent of these nonspecific types the lepromin test is positive, while in the other 40 to 60 per cent the lepromin test is negative. Therefore the nonspecific types may progress to the severe lepromatous manifestations or slowly develop the more benign tuberculoid symptoms.

From the Department of Dermatology and Syphilology, University of Havana, Service of Dr. V. Pardo-Castello.

Read before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Report of the Leonard Wood Memorial Conference on Leprosy, Internat. J. Leprosy **2:** 329 (July-Sept.) 1934.
2. Resolutions and Reports of the International Congress of Leprosy Held in Cairo, Egyptian M. A. **21:** 138 (March) 1938.
3. Rabello, Eduardo, Jr.: Una clasificação clinica-epidemiologica das formas da lepra, Rev. brasil. de leprol. **4:** 375, 1936.
4. Rabello, Eduardo, and Rabello, Eduardo, Jr.: Une classification clinico-epidermiologique des formes de la lèpre, Rev. brasil. de leprol. **6:** 229 (Sept.) 1938.
5. Schujman, S.: A propósito de una nueva clasificación de la lepra, Rev. brasil. de leprol. **8:** 111 (June) 1940.
6. Greco, Nicholas V.: Clasificación de la lepra, Rev. brasil. de leprol. **8:** 301 (Sept.) 1940.
7. Souza, Lima L.: Classificação das leprides, Rev. brasil. de leprol. **6:** 63, 1938.
8. Moura Costa, H.: Letter to the editor, Rev. brasil. de leprol. **8:** 202 (June) 1940.
9. Aguiar Pupo, J.: Das formas clinicas da lepra, Rev. brasil. de leprol. **7:** 357 (Dec.) 1939.
10. Baliña, P. L., and Bassombrio, G.: Classificación des formes cliniques de lèpre, Rev. brasil. de leprol. **6:** 225 (Sept.) 1938.

The accompanying table resumes the South American classification of leprosy modified by us, to make the clinical aspects more prominent and adding the lazarine type of tuberculoid leprosy.

THE LEPROMATOUS TYPES

When Mycobacterium leprae invades the skin, mucous membranes, peripheral nerves and other tissues and organs, finding little or no defensive reaction, the histologic features are those of a chronic infiltrating granuloma affecting the totality of the tissue. The cells are large histiocytes with special characteristics; some are vacuolated and badly stained and some are huge cells filled with mucous degenerated protoplasm and innumerable accumulations of acid fast bacilli. The connective and elastic tissue disappear entirely and are supplanted by the cellular infiltrate. The glands and hair follicles are gradually choked and finally atrophy.

These infiltrations appear clinically as nodular formations, more or less lobulated, usually dark red, well defined from the adjacent parts and varying in diameter from a few millimeters to several centimeters. Others are diffuse infiltrations without definite outline, more or less flat and geographic in outline. In the peripheral nerves the infiltrations may be total, thickening the nerves to three or more times their normal size, or may be moniliform, like the beads of a large rosary along the trunk of the nerve. In other tissues such as the testicle and mammary gland the lepromas affect the form of hard nodules, absolutely painless and without apparent signs of inflammation. In the larynx, nose and other mucous membranes the lesions ulcerate early, and deformities and mutilations are extreme. In advanced cases lesions of the liver and other internal organs present the same diffuse lepromatous infiltrations or localized nodular formations.

This is the easiest type to diagnose, and the cutaneous lesions may be recognized even by the layman in countries where leprosy is common.

Bacteriologically the lepromatous lesions are so full of acid fast bacilli that in the tissues they may be seen with the small dry objective in the form of bright red patches spread throughout the microscopic field. Two methods may be employed to examine tissues for bacteriologic diagnosis: one may remove a piece of a leproma by means of small curved scissors, imprinting the tissue juices on several cover slides, or make a small incision in the mass of the leproma, scraping off the soft tissues in the bottom of the wound with the scalpel and spreading the juice thus obtained on a cover slide. When proper staining is done by the Ziehl-Neelsen method, the number of acid fast bacilli in these preparations is enormous. It must be remarked that the specimens obtained from the mucous membranes of the nose should be taken by scraping the mucosa as deeply as possible without causing hemorrhage.

Immunologically lepromatous types show absolutely no reaction when tested with lepromin. Sometimes an early nonspecific reaction appears after the first or second day but disappears without leaving any trace. This absence of allergic response to lepromin means that the patient offers no defense to the infection. Therefore the prognosis of these cases is bad.

From a prophylactic point of view, lepromatous cases are dangerous, being open and literally oozing Mycobacterium leprae of the highest virulence. These are the cases that must be isolated from the community.

THE TUBERCULOID TYPES

The tuberculoid types show three different histopathologic variations: the typical miliary type with giant cells, the sarcoidal type with circumscribed collections of hystiocytes of the foamy type in the form of round, oval or sausage shaped nests and a third type with peculiar features ending in necrosis, which we have described as "lazarine leprosy."[11] In the peripheral nerves the histologic changes are similar and there is a particular type reported by Eduardo Rabello Jr.[12] as "nodular colliquative neuritis" in which necrosis and abscess formation are the main features together with typical tuberculoid follicular structure. This last mentioned type may possibly be the neural equivalent of the "lazarine leprosy" of the skin.

Eduardo Rabello Jr.[13] has described tuberculoid changes of the sarcoidal variety in the lymphatic glands and bones, a syndrome difficult to differentiate from lymphogranulomatosis benigna or Besnier-Boeck-Schaumann disease.

Clinically the tuberculoid lesions of the skin and peripheral nerves may be diagnosed by the expert. As a rule the lesions are few in number, sharply circumscribed, erythematous patches or flat infiltrations, often ring shaped or festooned, with macular center and elevated border, the latter being uniform or composed of small nodules arranged side by side.

Sometimes the lesions, which are first infiltrated and elevated patches of vivid red or purple, suffer a process of involution in the center and become atrophic with a ringlike border. The nerves more often affected are those of the upper extremities, particularly the ulnar, and also the superficial auricular branch of the cervical plexus. They appear as thick, pencil-like, lineal infiltrations under the skin but show no discoloration. The ulnar nerve may be palpated in the ulnar canal at the inner part of the elbow as a thick or moniliform cord. In the type described by Eduardo Rabello Jr., of which we have seen only 1 case, the painless abscess forms in the mass of the ulnar nerve and progresses toward the skin, adhering to the latter and finally causing superficial necrosis and ulceration.

Bacteriologically the lesions of tuberculoid leprosy show very few acid fast bacilli. Often only one or two bacilli may be seen in a whole section of skin or nerve after painstaking search. Often no bacilli at all can be demonstrated, either in the sections or in the lymph, tissue scrapings or mucous membrane secretions.

Immunologically the tuberculoid types of leprosy show the maximum possible allergy of the skin in the form of strongly positive lepromin tests, varying from the nodular to the necrotic. This is a constant feature which shows the excellent defenses of the body and proves once more the law of Jadassohn-Lewandowsky.

From a prophylactic point of view, persons with tuberculoid leprosy are not dangerous and in some countries where leprosy is endemic these patients are not isolated but are allowed to remain at home under sanitary supervision. Some leprologists contend that these patients should not be treated but allowed to develop their immune reactions spontaneously.

11. Pardo-Castello, V., and Caballero, G. M.: Lazarine Leprosy: A Peculiar Monosymptomatic Form of Leprosy, Arch. Dermat. & Syph. **23**: 1 (Jan.) 1931.

12. Rabello, Eduardo, Jr.: Etiologie générale et pathogénie de la lèpre tuberculoide, Rev. brasil. de leprol. **6**: 291 (Sept.) 1938.

13. Rabello, Eduardo, Jr.: Données nouvelles pour l'interprétation de l'affection de Besnier-Boeck; rôle de la lèpre, Ann. de Dermat. et Syph. **7**: 571 (June) 1936.

In "lazarine leprosy" the clinical lesions consist of plaques of cutaneous gangrene developing at the site of bullae; these necrotic manifestations are few in number but extremely destructive, causing deep, foul ulcers usually in the extremities, which disorganize the muscles, tendons and joints. These ulcers are painless and as a rule heal, leaving irregular scars in which there is absence of thermic and painful sensations. Recurrent crops of bullae may occur after healing. These are the only clinical manifestations, there being no other cutaneous or neural lesions of tuberculoid type. The peculiar feature of this type of tuberculoid leprosy is that in spite of the tuberculoid structure of the affected tissue the gangrenous parts and the contents of the bullae are extremely rich in Hansen bacilli but not the tissue. The lepromin test is strongly positive, showing a high allergic reaction indicative of excellent defenses. In our opinion the "lazarine" type of leprosy is the result of a massive infection with Hansen bacilli of patients with high immunologic defenses and the clinical symptoms represent the typical Koch phenomenon, with the throwing off of huge numbers of Hansen bacilli by the defensive mechanism of the body. Lazarine leprosy, although highly destructive, is of good prognosis and most patients recover spontaneously.

THE NONSPECIFIC TYPES

Clinically the nonspecific types of leprosy are characterized by the presence of macular, erythematous, achromic or pigmented skin lesions and by slight enlargement of the peripheral nerves with areas of apparently healthy skin in which the thermic and painful sensations are abolished. These types are at times exclusively neural and then the sole manifestations may be those due to trophic disturbances, such as areas of anesthesia, muscular atrophies, retraction of the fingers and toes, paralysis of the muscles of the face, bone reabsorptions, mal perforans plantaris, disturbances of the sweat and sebaceous secretions and falling of the hair. More often neural disturbances and cutaneous erythematous or dyschromic lesions are present together. Pathologically the tissues show only perivascular and perineural simple inflammatory changes consisting of cuffs of lymphocytes around the larger vessels of the upper cutis or the small trunks of the cutaneous nerves. In the cutaneous dyschromic or erythematous manifestations often called "leprids" there is also pronounced vascular dilatation and passive congestion. The basal cells are often devoid of pigment, and chromatophores may be very abundant on the upper cutis in the pigmented lesions.

Bacteriologically these lesions, whether of the skin or of the nerves, are poor in acid bacilli. As a rule direct examinations of lymph result in negative findings.

The lepromin test is negative in some cases and positive in others, about 50 per cent of each, although some investigators claim the numbers of positives much higher.

In reality cases of "nonspecific" leprosy are transitional types, some of which progress toward the "lepromatous" type and others toward the "tuberculoid" types. At times the transition is quite rapid, and a patient who showed only macular lesions will suddenly develop crops of lepromas in an acute outbreak of "lepra reaction."

The prognosis of these transitional types may be foretold by the results of the lepromin test. Those who show positive tests will probably remain as nonspecific types or will develop tuberculoid lesions. Those showing a negative lepromin reaction will in all probability develop lepromatous lesions.

THE MIXED TYPES

These transitions naturally result in types in which both lepromatous or tuberculoid and nonspecific "leprids" coexist until the patient finally develops the definite type which the disease will follow in his particular case. Therefore in these cases the presence of leproma establishes the type as "lepromatous" in spite of the presence of numerous erythematous or dyschromic lesions. Likewise the presence of tuberculoid lesions establishes the type as "tuberculoid" in spite of the presence of erythematous or dyschromic manifestations. In many cases the clinical appraisal may be difficult and resort must be had to pathologic and bacteriologic examinations and even to the lepromin test in order to classify a case in the proper type.

The presence of lepromatous and tuberculoid lesions in the same patient has not been observed by us. The transformation of a lepromatous type into a tuberculoid type or vice versa has been reported by several investigators, but we have not seen this phenomenon.

LEPRA REACTION

In sharp contrast with the usual slow and insidious evolution of leprosy there is sometimes observed an acute inflammatory phase which very frequently interrupts its chronic course or is the first clinical manifestation of the disease.

The major characteristic of the lepra reaction is its acuteness, more or less accentuated in different cases. It is probably a manifestation of allergy or hypersensitivity of the body to the pathogenic agent. Sometimes the outbreak of the lepra reaction can be ascribed to a definite cause: complicating diseases, alimentary or alcoholic excesses, too intensive antileprotic treatment, and so on. Frequently it is impossible to determine its cause. The clinical picture and evolution of lepra reaction differ in lepromatous and tuberculoid cases.

In lepromatous leprosy it generally begins suddenly with fever (39 to 40 C., or 102.2 to 104 F.), rigors, arthralgias, headache or prostration, followed in several hours by an eruption of erythema multiforme or erythema nodosum type and the exacerbation of preexisting lesions. In some cases there are extracutaneous symptoms: adenitis, orchitis, splenic and hepatic enlargement, neuritis and keratitis. The fever, of remitting type, and the other symptoms persist during several days, ten to fifteen, rarely more, and then disappear in lysis. Relapses are frequent. The lepromin test is negative. The erythrosedimentation index is greatly augmented. Short, acute reactions are of good prognostic significance.

Long or relapsing reactions aggravate the course of leprosy.

The first therapeutic measure is the cessation of all antileprotic treatment and the administration of a mild saline laxative and a bland diet.

Injections of antimony and potassium tartrate 1 per cent solution, calcium salts, vitamin B_1 and diphtheria toxoid are useful agents.

Exacerbations in tuberculoid leprosy are not accompanied by any general symptoms or fever. They are characterized by the turgescence of preexisting lesions, the appearance of new wine red, infiltrated patches

mostly located on the face and extremities, by a protracted course, never less than three months, and frequently more than a year in length. The lepromin test is positive. The erythrosedimentation index is always low and prognosis is always good.

THE HISTAMINE TEST

The early manifestations of leprosy of the nonspecific or simple inflammatory type may be difficult to diagnose, although, if thermal and pain anesthesia are present, matters are simplified. However, many patients, especially children, do not cooperate or they find it difficult to express their sensations, in which event the performance of the "histamine test" is very valuable.

When a drop of a 1:1,000 solution of a histamine salt is placed on the normal skin and a needle prick is made through the liquid, a small wheal surrounded by an erythematous halo develops within a few seconds and persists for five minutes or more. When the sensitive nerve endings are paralyzed or destroyed, the phenomenon occurs as far as whealing, but no erythematous halo develops around the wheal. The normal response to histamine is called the "positive test"; the absence of erythematous reaction around the wheal characterizes the "negative test." Therefore in the cutaneous lesions of leprosy the histamine test is always negative. We have found occasion to do this test in numerous cases in which erythematous or dyschromic lesions were suspected of being early manifestations of leprosy. The superficial, erythematonodular, cutaneous syphilids have been the subject of differential diagnosis with early lesions of leprosy in several cases, and in these the "histamine test" has proved of definite help. The serologic reactions may be positive in the presence of leprosy, and the changes in cutaneous sensations may be difficult to appraise when patients are not cooperative.

THE LEPROMIN TEST (MITSUDA REACTION)

The lepromin test consists essentially in the intradermal injection of an antigen prepared from lepromatous tissues rich in Hansen bacilli.

Skin tests in leprosy were originally intended to find a diagnostic procedure similar to the tuberculin test in tuberculosis. No results were obtained in this direction, and investigations were given up until 1923, when Mitsuda [14] reported that, when an emulsion prepared with lepromatous skin was inoculated, healthy persons gave positive results, maculoanesthetic patients presented a late, nodular persistent inflammation and tuberous patients gave a negative local reaction. He deduced from his experiences that persons without leprosy and maculoanesthetic patients had a special immunity to the infection, while tuberous patients had no immunity. These findings and conclusions were later fully confirmed by many investigators.

All attempts to consider the test of any value in diagnosis are definitely abandoned. Its great importance in the classification of cases of leprosy and its immunitary and prognostic value are actually recognized by all.

Lepromin is prepared by boiling lepromatous tissues in isotonic solution of sodium chloride for one hour. The mass is then ground up in a mortar, and 20 cc. of isotonic solution of sodium chloride is added for each gram of ground up tissue. After thorough mixing and grinding again, the supernatant fluid is pipetted off, filtered through gauze and stored in a sterile container, the remaining tissue being discarded.[15]

The liquid is autoclaved at 120 C. for fifteen minutes, phenolized at 0.5 per cent and distributed in insulin type vials ready for use. It is a cloudy, milky emulsion containing numerous bacilli and globi plus all the tissue elements of the leproma. Kept in a dark, cool place, it retains its activity for a long time. No easy standardization of lepromin is possible, being as it is such a complex suspension of bacilli and tissue material, but this does not interfere with the accuracy of results, as wide variations in the concentration of the antigen do not give correspondingly different reactions. A nonreacting patient to the usual lepromin will not react to an antigen two or three times stronger. A reacting patient will do so to dilutions as high as 1:3,000 of lepromin, although with less intensity.

The presence of bacilli is essential to the activity of lepromin. Filtered antigens are inactive. Lepromins

Positive lepromin test twenty-eight days after inoculation with 0.1 cc. of lepromin intradermally.

prepared with tuberculoid tissues (paucibacillary) produce attenuated reactions and then only in patients with strong reactions to the usual lepromin. Antigens prepared with normal skin are inactive.

The test is performed by injecting into the cutis 0.1 cc. of lepromin. The most common sites used are the arms, the dorsum and the anterior surface of the thigh. At the end of twenty-four to forty-eight hours an erythematous halo may be observed, with at times some infiltration; but these manifestations disappear quickly, usually after the fifth day, leaving a dark brown discoloration and some wrinkling of the skin. On the seventh to the tenth day a small papule begins to form in the positive cases, gradually increasing in size and reaching its acme about the third to the fourth week, when it may be a nodule of as much as 1 cm. in diameter. Occasionally the center sloughs off and a small ulcer

14. Mitsuda, K.: Troisième Conference internationale de la lèpre, Communications et Débats, Paris, J. B. Baillière et Fils, 1924, p. 219.

15. Rotberg, A.: Some Aspects of Immunity in Leprosy and Their Importance in Epidemiology, Pathogenesis and Classification of Forms of the Disease, Rev. brasil. de leprol. **5**: 45 (special number) 1937.

forms which requires several weeks to heal. In most cases the nodule regresses gradually after the fourth week, but in some cases of positive reaction some scarring is left. Rarely a positive reaction may not show until the third or fourth week and then follow the usual regressive course.

The erythematous reaction of the first few days is considered nonspecific. The reading of the test should be done about the thirtieth day after the intradermal injection. If there is no reaction or only a small (less than 5 mm.) infiltration the test is negative. A well formed nodule more than 5 mm. in diameter with or without a necrotic center characterizes the positive test.

Microscopic examination when the Mitsuda reaction is positive shows in specimens removed at its acme a collection of histiocytes, lymphocytes and at times giant cells, with an aspect very similar to that of tuberculoid leprosy. In specimens removed forty-eight hours after inoculation acute inflammatory phenomena may be observed without any specific changes, but in some of our specimens a decided perivascular histiocytic infiltration was present, resembling even at this early date the tissue changes of tuberculoid leprosy. However, we do not believe this is of diagnostic significance, as we have observed similar changes in lepromin tests of forty-eight hours' duration which later proved to be negative. The injected bacilli are not demonstrable in the lepromin reacting tissues. In negative tests, after the initial inflammatory reaction biopsies performed after eight, fifteen and twenty-eight days showed a return of the tissues to normal.

COMMENT

1. The classification of the types of leprosy on a histopathologic foundation into "lepromatous," "tuberculoid" and "nonspecific" is the result of studies made by dermatologists of Brazil and Argentina, and accepted by Latin American dermatology. In this article an attempt is made to correlate these pathologic forms with the clinical, immunologic, bacteriologic and public health aspects of the disease.

The lepromin test is given an important place among the immunologic reactions of the skin and reports are made based on many tests performed by the authors, corroborating for the most part the findings of other investigators.

The histamine test is studied as a diagnostic procedure in early cases of leprosy with lesions of the "nonspecific" type.

Consulado 9.

ABSTRACT OF DISCUSSION

DR. HOWARD FOX, New York: The authors have done well to call attention to three phases of leprosy which are apparently not well known to American dermatologists. Little is said about them in American textbooks on dermatology or even in books on tropical medicine. I refer to the South American classification, the lepromin reaction and the histamine test. The classification of leprosy adopted at the Memorial Conference in Manila in 1931 divided the types of the disease into cutaneous, neural and mixed. They used the symbols C and N, adding the numbers 1, 2 or 3 according to the severity of the individual case. This classification was not satisfactory, as the cutaneous lesions are of two entirely different types. One of them, long known as nodular, represents a severe and usually fatal type, whereas the maculoanesthetic and the tuberculoid lesions represent a relatively benign type and are invariably seen in neural leprosy. An improvement in classification was made at the International Congress of Leprosy in Cairo in 1938 by changing the term cutaneous to lepromatous and by including as subtypes of neural leprosy the pure anesthetic, the maculoanesthetic and the tuberculoid forms. The classification adopted by South American leprologists, while not as simple as those aforementioned, has the advantage, as the authors say, of correlating the clinical appearance of the disease with the pathologic, bacteriologic and immunologic changes. The nonspecific group is convenient, as one is at times doubtful as to whether macules are forerunners of the lepromatous type or of the relatively benign neural type of the disease. In such cases it may be impossible to settle the question by either microscopic or bacteriologic examination, but this can be done by the lepromin test. Tuberculoid leprosy, first described by Jadassohn, is invariably associated with the neural type of the disease. It shows a tuberculoid structure histologically with few, if any, bacilli and gives a positive lepromin reaction indicative of comparative immunity to the bacilli. This type may often be recognized from the clinical appearance alone, the lesions being sharply defined, more or less asymmetrical and often bright red. Some of them appear as large coin to palm sized, yellowish, slightly thickened patches often with a mammillated surface. Others appear as diffuse, slightly thickened areas with a raised border and a tendency to form circles or portions of circles. The so-called lazarine type of leprosy, which the authors have added to the South American classification, is a rare manifestation, the only examples which I have seen being those which Dr. Pardo-Castello demonstrated at the meeting of the American Dermatological Association in Havana in 1932. Curiously enough, in spite of the destructive character of the lesions the lepromin reaction is always positive, which indicates a good prognosis as to life.

DR. MARION B. SULZBERGER, New York: Drs. Castello and Tiant give an insight into the immunologic-biologic relationships in leprosy with a degree of clarity never previously offered to an American audience. The immunologic-biologic factors in leprosy were studied first and most extensively by Josef Jadassohn while in Berne, Switzerland. There is an endemic focus of leprosy in Switzerland in several extremely isolated valleys of the canton of Valais. Few physicians from the outer world have penetrated into these valleys. At the time of Jadassohn's investigation leprosy had been in existence in these valleys for many generations. The peculiar thing is that leprosy has never disseminated from that focus to anywhere else in Switzerland. This brings out a well known factor, namely that climatic and environmental conditions have a great deal to do with the transmission of leprosy. A person with leprosy was discovered somewhere in the southern part of Germany. The German government did not know what to do with him. They put him in a freight car and shoved food and water within his reach. They then shunted this freight car from train to train and they got it across the Swiss border. Jadassohn was called to see this poor man, whom he took to his hospital and even to his home and studied him intensively. Jadassohn thus established his concept of tuberculoid leprosy and came to the conclusion that not only was the lepromin test positive in this tuberculoid form of leprosy but also that it was impossible in this particular case to find the bacilli. These findings in leprosy were a further support of the Jadassohn-Lewandowsky law, which had been developed particularly in relation to tuberculosis, syphilis and fungous infections. This law states that, wherever the immune mechanisms of the host are sufficiently active and adequate to produce a diminution of micro-organisms or their virulence within the tissues of the host, tuberculoid structures may appear. In this law there is an explanation of a great many facts known in tuberculosis and, more important still, it clarifies the morphologic and immunobiologic relationships not only in regard to tuberculosis but also in many other chronic granulomatous infections, such as leprosy, syphilis and certain fungous infections. There are many differences between these diseases, but their fundamental relationship lies in the fact that the way in which the host reacts is due to his immunologic-biologic status at the time his tissues encounter the products of micro-organisms to the specific local status and general status. These specific immunobiologic states determine (1) the histology of the lesion (tuberculoid structures or nontuberculoid structures), (2) the number of bacilli present (rare or numerous), (3) the course of the disease (its prognosis, good or bad), (4) the contagiousness of the disease (which is to some measure, at least, a corol-

lary to the bacillary findings) and (5) the type of treatment and sometimes the response to the treatment. All these five follow immunobiologic laws which are now clearly discernible not only in leprosy and tuberculosis but in innumerable other infectious diseases as well.

DR. ALFRED HOLLANDER, Springfield, Mass.: I should like to ask Dr. Castello what experience he has had with the following method: During the time of my association with Unna in Hamburg we always tried to find bacilli with the solidified carbon dioxide method, especially in nonspecific cases, when we could not find them by any other method. We put solidified carbon dioxide on the skin and produced a blister, and often when in these nonspecific cases we were unable to find any bacilli by other methods we found them by this method. Dr. Sulzberger mentioned the work of Jadassohn. I should like to call attention to the fact that Dr. Paul G. Unna has worked on leprosy since 1875. He has done some quite important work, especially on the histopathologic part of leprosy. He went to his friend Hansen in 1876 and after that he treated leprosy in his clinic in Hamburg. We always had between 10 and 20 patients, mostly from South America, isolated in our leprosy department.

DR. PAUL GROSS, New York: It is a privilege to express admiration for Dr. Castello's presentation of the problems of leprosy and for his contributions to dermatology in general. One only need recall his paper on venereal lymphogranuloma published in 1926 to appreciate the tribute due to him and to the medical profession of South America in general. The distribution of the positive lepromin test among the various types of leprosy, as shown by Dr. Castello, seems to correspond in certain respects to the luetin test of syphilis. A positive luetin reaction seemed to depend on the development of the allergic state of tertiarism with its pronounced tissue reaction and absence of spirochetes in the tertiary lesions. Similarly, the lepromin test is specific for the tuberculoid types of leprosy, which are distinguished by their tissue reaction and an absence or scarcity of lepra bacilli. It would be interesting to hear from Dr. Castello whether the lepromin test can be used to differentiate between sarcoid leprosy and sarcoidosis of tuberculous origin.

DR. GUY H. FAGET, Carville, La.: As yet in the United States we have not adopted this classification, but I can see that at the next International Conference on Leprosy it may possibly be adopted. I can see many valuable points in this new classification originated by the South American leprologists. As I understand it, we might consider the maculoanesthetic leprosy, or what the South American leprologists call the nonspecific type of leprosy, as the transitional form, or the intermediate form between the more severe lepromatous type and the more benign tuberculoid type of leprosy. In the lepromin test, therefore, we have a significant and valuable prognostic test for the differentiating of the types of the disease. With this new world war and our American boys going into tropical countries there is a grave possibility of a large increase in leprosy in the United States. At the national leprosarium at Carville we are ready to take care of such additional cases, as we have the facilities there for the hospitalization of 480 patients and can make room for more if necessary.

DR. FRED D. WEIDMAN, Philadelphia: A large part of the merit of the South American classification lies in what Dr. Castello indicated, namely that thereby one can tie in certain of the newer features of leprosy with what we have always thought we knew about the morbid anatomy (the "dermatology") of the condition. But morbid anatomy is not everything. It is in the nature of medicine at large to develop especially along bacteriologic, immunologic and public health lines, and with such newer developments in leprosy the older classification has become more or less obsolete. At least it has been necessary to contrive some sort of an additional classification, not necessarily a new classification, but an auxiliary classification whereby these "basic science" aspects of leprosy may be reconciled and tied in with the morbid anatomy. Dr. Castello did not have time to elaborate on a certain sentence in the printed paper which I think he may care to dwell on in his closing discussion, in which he speaks of the worthlessness of the lepromin test. That would seem to be contrary to what we have heard this morning. It would appear on the face of it that in the lepromin test, as Dr. Gross stated, we have at once a valuable method for distinguishing tubercular leprosy from puzzling cases of sarcoid. This is the aspect of leprosy which gives me the greatest difficulty in differential diagnosis. I should like to have Dr. Castello say something too about the frequency of lazarine leprosy. I am sorry that he did not show a lantern slide of that condition. It does not look like leprosy at all. Certainly it is rare in the United States. I should like to have Dr. Castello tell us whether it is likewise rare in Cuba. When I read the paper there was one place where my mind stumbled, and that was with respect to the use of the term "follicular" as employed in connection with the histology. When one says "follicular" to the general pathologist one thinks of such structures as the cortical follicles in the lymph nodes, and to the dermatologist the term "follicular" would conjure up thoughts of a hair follicle. The general pathologist prefers the term "miliary." In tuberculosis we speak of "miliary tubercles" to indicate those which are sharply circumscribed. I take it, though, that Dr. Castello's "follicular" is a literal translation from the Spanish and Portuguese, but perhaps it will conduce to clarity in North America if we might substitute the term "miliary."

DR. V. PARDO-CASTELLO, Havana, Cuba: I want to thank you for this generous discussion. We have performed hundreds of lepromin tests on all types of patients and also on healthy men. We find in Cuba that all healthy men and women are lepromin positive. In other words, we live in a leprous country, we have been in contact with leprous persons for many years and we have developed immunity to leprosy; therefore our lepromin tests, my associates' and mine, are positive. We are trying to get hold of a number of Europeans who have not been in contact with leprosy, and we are in contact with the immigration authorities in Cuba in order to perform lepromin tests on this type of men. Probably they will show negative, since they have not been in contact with leprosy. In reply to Dr. Hollander, we have tried, and so have all leprologists, to recover bacilli from the nonspecific types and the tuberculoid types by every method. Of course, some have been found but always in small quantities and in some cases it has been absolutely impossible to prove their existence. As far as sarcoid and tuberculosis are concerned, I must recall to your minds that Dr. Balina of Buenos Aires and Dr. Rabello of Rio de Janeiro have reported cases of sarcoid caused by leprosy. Whether it is tuberculosis or a filtered virus we don't know, but sarcoid disease due to leprosy with the typical skin lesions, clinically and pathologically and with lesions of the lymph nodes and lesions of the small bones of the extremities is indistinguishable from sarcoid of any other type. I do not believe that we can use the lepromin test to differentiate between these cases because, as I said before, all Cubans are lepromin positive when they do not have leprosy of the lepromatous type, and therefore a case of sarcoid in Cuba or in any native of a country where the leprous abound would be lepromin positive. I want to emphasize that lepromin is not a diagnostic test. All attempts to make a diagnostic test with lepromin have been abandoned. It is a prognostic test and in that light is a very useful test. Dr. Weidman is right about the word "follicular." In Spanish and in Portuguese we call "follicular" that type of tuberculosis which you call here "miliary." It would perhaps be a good idea to change from "follicular" to "miliary." I believe the lazarine type of leprosy is a special type of tuberculoid leprosy; that is, these patients are lepromin positive and yet they have an enormous amount of bacilli in the necrotic part of the lesions, not in the tissues themselves. I interpret that as the Koch phenomenon in the case of leprosy the same as you would obtain in a case of tuberculosis with massive injection of tubercle bacilli when there already is a certain amount of immunity against tubercle bacilli. It is the massive infection somehow introduced into the system of the man who has high immunity and high defensive powers against leprosy and therefore the local lesions of the necrotic, destructive type and the good prognosis with the positive lepromin test.

EVALUATION OF ANGIOCARDIOGRAPHY

HENRY K. TAYLOR, M.D.
Roentgenologist, Goldwater Memorial Hospital
AND
TERESA McGOVERN, M.D.
Visiting Physician, Columbia Medical Division, Goldwater Memorial Hospital
WELFARE ISLAND, N. Y.

This report summarizes the examination of 100 persons by the Robb-Steinberg method.[1] The patient material comprises the groups included in the accompanying table. Many of the patients suffered from other ailments, such as hemiplegia due to hypertensive cardiovascular disease, diabetes mellitus, nephritis and the like. However, this report is limited to the angiocardiographic study of the heart and major blood vessels.

TECHNIC

The angiocardiographic technic described by Robb and Steinberg was employed throughout the course of this study.

Patient Material for Evaluation of Angiocardiography

Types	Patients
Normal	18
Rheumatic heart disease	20
Arteriosclerotic heart disease	15
Hypertensive heart disease	20
Congenital anomalies	4
Aneurysms	11
Chronic intrapulmonary disease	10
Syphilitic heart disease	1
Pulmonary endarteritis	1
Leukemia	1
Tabes dorsalis	1
Total	100

Circulation time tests were determined by injection of solutions of ether, macasol,[2] dehydrocholic acid, sodium cyanide and saccharin. The results of these studies enabled us to calculate approximately the time at which the radiopaque substance would arrive at various locations.

A 70 per cent solution of diodrast (30 to 50 cc.) was injected intravenously and films were taken at predetermined intervals. Two such injections were found necessary for satisfactory visualization. In some patients three were required. Approximately fifteen minutes were allowed to elapse between injections. With each injection two exposures were made in the erect position at a distance of 6 feet. In several cases this entire procedure was repeated on one or two subsequent dates. For the average examination, excluding the preliminary films, four films were utilized, two in the posteroanterior position and two in an oblique position, thus obtaining roentgenograms of the right and the left side of the heart in each position. In addition to these tests, a few patients were examined in the supine position with the Bucky diaphragm at 36 inches.

All our observations are based on the technic described. At the present time we believe that this is sufficient for practical purposes. We believe, however, that much more information could be obtained through multiple serial exposures, as described by Sussman,[3] and from motion pictures of the fluoroscopic screen.

REACTIONS TO DIODRAST INJECTIONS

Reactions to the injections of diodrast, which at no time were alarming, were as follows: Immediately after the injection, each patient experienced a flushing of the head and neck, in addition to a profound sense of warmth throughout the entire body. Most of the patients salivated profusely, some became nauseated and others had coughing spells. All these symptoms, however, disappeared quickly. Emesis was noted only in those patients who had eaten prior to the injection. In some cases there was an urgency to urinate or to defecate, but in no instance did incontinence occur. A sense of weakness invariably accompanied or followed the procedure. Immediately after the injection the blood pressure dropped. In some cases the systolic drop was as much as 80 mm. of mercury, and the diastolic drop from 50 to 60 mm. The hypotension, however, was of a transitory nature with a return to the preinjection level within five minutes and at the same time a disappearance of the sense of weakness.

Itching and urticarial rashes appeared in a few cases, increasing in intensity after the second injection. All were relieved by subcutaneous injection of epinephrine. None of the persons had been previously tested for sensitivity. Of all the patients examined, 21 were subsequently given cutaneous tests for sensitivity. Sensitivity was determined by injecting intradermally 0.2 cc. of a 70 per cent diodrast solution into the volar surface of the arm. The wheal raised by this injection was measured and the area observed at ten minute intervals for an hour. Of this group, 6 showed positive reactions within fifteen minutes; the others showed no reaction for more that one hour. A reaction was considered positive when the wheal, erythema and pseudopodiums measured more than 2.5 cm. in diameter. Some of these reactions appeared almost immediately; others did not appear for fifteen minutes.

The development of sensitivity to the contrast substance is a possibility and should not be overlooked.[4] From the 21 patients tested there seems to be little or no correlation between the degree of sensitivity to an intradermal test with 0.2 cc. of 70 per cent diodrast and the reactions experienced at the time of the intravenous injection of 30 to 50 cc. of the 70 per cent diodrast. In 20 cases the injected vein became thrombosed within forty-eight hours but was subsequently recanalized.

ANATOMY—NORMAL HEARTS

Our examinations have shown variations from the recognized and accepted radiographic anatomy of the cardiac silhouette in the normal as well as in the abnor-

The Nepera Company supplied the macasol and the Winthrop Chemical Company the diodrast.

From the Roentgen Ray Department and Columbia Medical Division, Goldwater Memorial Hospital.

Read before the Section on Radiology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Robb, G. P., and Steinberg, I.: Visualization of the Chambers of the Heart, Pulmonary Circulation and Great Vessels in Man: Practical Method, Am. J. Roentgenol. **41**: 1-17 (Jan.) 1939.

2. Macasol is a solution containing magnesium sulfate, calcium gluconate, sodium chloride and copper sulfate in distilled water (Spier, L. C.; Wright, I. S., and Saylor, Leslie: A New Method for Determining the Circulation Time Throughout the Vascular System, Am. Heart J. **12**: 511-520 [Nov.] 1936).

3. Sussman, M. L.; Steinberg, M. F., and Grishman, Arthur: A Multiple Exposure Technic in Contrast Visualization of Cardiac Chambers and Great Vessels, Am. J. Roentgenol. **46**: 745-747 (Nov.) 1941.

4. Goldburgh, H. L., and Baer, Samuel: Death After the Intravenous Use of Diodrast, J. A. M. A. **118**: 1051-1052 (March 28) 1942. Dolan, L. P.: Allergic Death Due to Intravenous Use of Diodrast, ibid. **114**: 138-139 (Jan. 13) 1940. Crane, J. J.: Sudden Death Following the Intravenous Administration of Diodrast, J. Urol. **42**: 745-748 (Nov.) 1939.

mal. The present study indicates that existing concepts concerning the size, shape and position of the heart chambers and the thickness of its muscles are different from those observed in the adynamic viscus in the cadaver. Our concepts require modification in the light of observations made in vivo on the dynamic viscus.

Posteroanterior Position (fig. 1 *A*).—In this position, with contrast substance opacifying the superior vena cava, the right auricle, the right ventricle, the conus, the pulmonary aorta and the right and left pulmonary arteries, the entire right side of the heart appears to be a U shaped structure. The upper part of the right arm of the U is the superior vena cava and the lower part is the right auricle. When these two structures are combined they form the right border of the cardiac silhouette. In a number of instances we have observed a lack of filling with contrast substance in the right lower portion of the cardiac silhouette. This lack of filling when the right side of the heart is filled with contrast substance led to our excluding that portion as part of the right side of the heart. This region is therefore referred to as a silent area.

Pulsations with ventricular characteristics have been observed on kymographic examinations of this so-called silent area. Since we have also observed ventricular types of pulsations on that portion of the cardiac silhouette corresponding to the lower portion of the superior vena cava and the right auricle, we have concluded that the silent area is the site of the inferior vena cava and that the superior vena cava, the right auricle and the inferior vena cava are capable of transmitting ventricular pulsations.[5]

The right ventricle is represented by the horizontal part and the lower portion of the left upright arm of the U. The left arm of the U is superimposed on the spine and seldom extends beyond the left lateral border thereof. The interventricular septum, or the left lateral border of the opacified right side of the heart, is vertical, with a tendency to convexity to the right. The apex of the right ventricle is usually represented as an acute angle far removed from the cardiac apex.

When the left pulmonary artery is outlined by contrast substance it is found to occupy only a small part of the left border of the cardiac silhouette, situated between the aortic knob and the superior portion of the left ventricle. The right ventricular conus does not participate in the formation of the left margin of the cardiac silhouette, and only rarely does the pulmonary aorta reach that margin; instead, these two structures are visualized deep within the cardiac shadow. The left pulmonary artery is below the thoracic aorta. At times, however, as the left pulmonary artery ascends, its left lateral border forms the lower part of the middle cardiac segment. The pulmonary aorta may be convex toward the left, and it may extend to, but not beyond, the left cardiac border.

The lateral dimension of the right side of the heart, in the posteroanterior position, as demonstrated with the aid of contrast substance, is considerably smaller than our previous conception of it. When enlarged, it does not approach the left border and is appreciably removed from the left lateral border of the cardiac silhouette.

When the left side of the heart is opacified the two chambers assume the shape of a figure 8, obliquely situated at about a 30 degree angle from the horizontal. The auricular shadow is circular in outline, forms no part of either border of the heart shadow and is disposed more to the right than to the left. In only 1 instance was the contrary observed. The ventricular shadow is more often seen to be oval, occupying the major portion of the left half of the heart, including the apex.

Further observations of the left cardiac border demonstrated that the middle segment (i. e., the area between the aortic knob and the base of the ventricle) might be composed of a part of the pulmonary aorta. The remainder of the border is a continuation of the pulmonary aorta at its bifurcation, as the left pulmonary artery. When the middle segment was not so composed, we found it to be made up, in whole or in part, by the descending portion of the left pulmonary artery or of the descending thoracic aorta as it descends and divides the cardiac silhouette.

In many instances there was a lack of filling with contrast substance of the lower portion of the middle cardiac segment, namely that portion above the base of the left ventricle. This is another so-called silent area, as it lacks contrast substance when the left side of the heart otherwise is filled. In only 1 instance did this area fill with contrast substance. The outline obtained led us to believe that this area is occupied by the left auricular appendage.

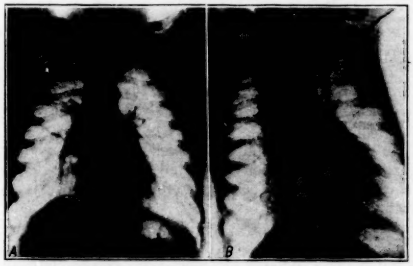

Fig. 1.—Normal heart. *A*, posteroanterior view showing entire right side of the heart opacified. No contrast substance is present in the lower right portion of the cardiac silhouette (silent area); apex of the right ventricle is seen considerably to the right of the cardiac apex. *B*, heart pervades only half of the cardiac shadow.

These examinations also revealed variations in the position of the ascending and the descending aorta. They have appeared superimposed, adjacent to and widely separated from each other. The ascending aorta rarely forms part of the border of the right side of the heart except when it is tortuous, elongated or dilated.

An aortic knob, not demonstrable by routine examination, can be demonstrated if present by angiocardiography.

Right Anterior Oblique Position (fig. 1 *B*).—In this view, the position of the U shaped right heart is somewhat similar to that observed in the posteroanterior position. The only appreciable variation is a greater separation of the limbs of the U. The superior vena cava is visualized as it enters the right auricle. The right ventricle forms the horizontal and ascending portion of the U. In some cases a constriction in the contrast substance demarcates the site of the tricuspid ring.

5. Schwarzschild, M.: Personal communication to the authors.

The left pulmonary artery transversely crosses the clear space between the upper portion of the arms of the U. The opacified right ventricle does not occupy more than half of the ventral cardiac shadow in this position. Heretofore a larger portion of the silhouette was attributed to this structure. The left ventricular shadow, on the other hand, occupies considerably more space than was previously believed.

Fig. 2.—*A*, left anterior oblique view showing the superior vena cava and the right auricle. *B*, left anterior oblique view showing the right side of the heart as a rectangular structure with anterior convexity occupying ventral half of the cardiac silhouette.

The left auricle and left ventricle form a figure 8 lying in an almost horizontal plane, with the auricular chamber at a slightly higher level than the ventricular chamber.

In this oblique position, the ascending and descending aortic shadows are not only parallel but also very close to each other, often being superimposed. There is no arch.

Left Anterior Oblique Position.—The U appearance of the right heart, as observed in the posteroanterior and right anterior oblique positions, now changes into an elongated rectangular structure as the two vertical arms of the U become superimposed (fig. 2). The right heart occupies the ventral portion of the cardiac silhouette and is convex anteriorly. The chambers are superimposed and cannot be differentiated. The posterior limit of the contrast substance, representing the interventricular septum, is convex to the right.

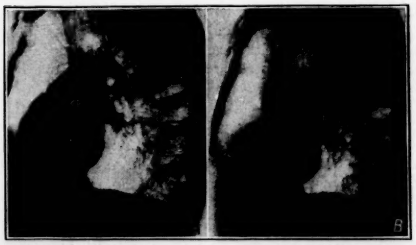

Fig. 3.—*A*, left lateral view showing the right side of the heart opacified. *B*, left lateral view showing the left side of the heart and aorta opacified.

In this position, the left heart forms a kidney shaped structure with a deep ventral concavity from the depths of which arises the aorta.

Lateral Position (fig. 3).—In this position, the outline of the right and left portions of the heart shows little variation from the contours found in the left anterior oblique position of a normal heart.

VARIATIONS FROM THE NORMAL

The facilities at our disposal permitted the obtaining of only two films for each injection with contrast substance. Under the circumstances we endeavored to obtain as much information as possible, arranging our examinations so as to get as much as possible of the cardiovascular portion of each side of the heart opacified with each exposure. Because of technical limitation it was not possible in all instances to differentiate one heart chamber from another. However, separate opacifications of each side of the heart were obtainable. In the remainder of our presentation we shall refer to the right and the left sides of the heart as separate units, each unit being considered a combined auricular and ventricular shadow. Whenever possible, we shall refer to the individual chambers.

Anatomic changes were apparent. There were variations in size and shape of the cavities and increased thickness of the cardiac muscle wall. These abnormalities could be readily differentiated from the variations normally occurring during systole and diastole.

Fig. 4.—*A*, left anterior oblique view showing dilated right heart. *B*, left anterior oblique view showing the left side of the heart with no demarcation between the left ventricle and aorta, indicating insufficiency factor.

Enlargement of the right heart chamber was manifested in the posteroanterior position by a generalized increase in the size of the U shaped structure with an advance of the interventricular septum to the left. The shift in the apical region was less pronounced than that in the area of the conus. In the left anterior oblique view, the right side of the heart when enlarged assumed the shape of an inverted mushroom. In our opinion this signified enlargement of the chamber. The greatest enlargement was observed in the lower and posterior portion of the right side of the heart. The interventricular septum, in the region of the apex, was, to a variable extent, convex to the left. This type of change was not necessarily accompanied by an increase in muscular thickness or by cardiac enlargement. It represented (or was interpreted as) simply chamber enlargement or dilatation without appreciable muscular hypertrophy or cardiac enlargement. Enlargement of the right side of the heart in some instances was present without the inverted mushroom appearance. In one type we observed the upper opacified area in the right side of the heart to be enlarged, whereas the lowermost,

or dependent, portion did not participate in the enlargement. The convexity of the interventricular septum occurred in either direction.

Enlargement of the left heart chamber could be visualized in all positions. The size and shape of the shadow determined whether the enlargement was auricular or ventricular and, if ventricular, whether the heart was in systole or diastole at the time of the exposure.

The left anterior oblique position yielded a characteristic roentgenogram. Whereas normally the left ventricle appeared as a small opacified sphere, when enlarged it manifested itself in one of two ways. In the first, the junction between the ventricle and the aorta was lost (fig. 4 *B*). This area was widened, the chamber was elongated and the entire configuration took on a tonguelike appearance, with the interventricular septum convex to the right. In the second, there was no loss of demarcation between the ventricle and the aorta. The chamber enlarged anteriorly, but the septal deviation remained convex to the right. The former enlargement is associated with an insufficiency or regurgitant lesion of the aortic valve; the latter with hypertension or obstructions at the aortic ring.

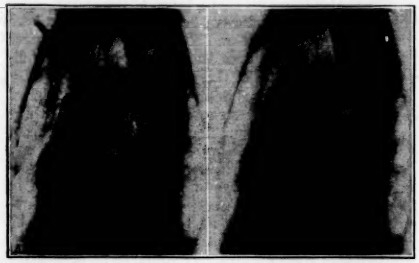

Fig. 5.—*A*, left anterior oblique view showing the right side of the heart opacified; cardiac hypertrophy. Clinically, hypertension, cardiorenal disease. *B*, same as *A*, showing hypertrophy of the left side of the heart.

The diagnosis of mediastinal lesions was considerably facilitated by the use of contrast substance. It was possible to differentiate between mediastinal tumors and vascular lesions in the mediastinum, conditions which are not always easily diagnosed by kymographic studies. Transmitted pulsations on a kymographic record may be interpreted as vascular pulsations. We have observed kymographic studies of aneurysms with no evidence of pulsations and, conversely, pulsations in mediastinal tumors. By angiocardiographic studies we were able to differentiate mediastinal lesions from aneurysms with only 2 exceptions. In 1 case we were able to recognize multiple aneurysms arising from the arch of the aorta and also locate a large mediastinal mass in the retrocardiac area. This mass displaced the esophagus anteriorly and to the right and eroded the spine. Not being able to demonstrate any contrast substance within this mass, we were led to diagnose it as a neurogenic tumor in addition to the multiple aneurysms. At autopsy the mass proved to be a large aneurysm containing a huge laminated clot with a small lumen for the passage of blood. This postmortem examination made it quite clear why kymography had shown no pulsations and why contrast substance had not been allowed to accumulate in sufficient concentration to cast a recognizable shadow. In another instance failure to demonstrate the aneurysm proved to be due to dilution of the contrast substance within a huge, diffuse dilatation occurring throughout the entire length of the descending aorta. Kymographic examination had revealed typical aortic pulsations synchronized with the aortic pulsations.

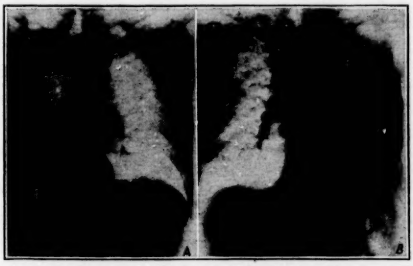

Fig. 6.—*A*, posteroanterior view showing definite retraction of the mediastinal structures to the right secondary to pleural and pulmonary fibrosis of the right lung, compensatory emphysema of the left lung. Right side of the heart opacified, plow shaped appearance. *B*, posteroanterior view showing definite retraction of the mediastinal structures to the left secondary to pleural fibrosis and bronchiectasis and compensatory emphysema of the right lung. Note enormous U shaped right heart.

The distribution of the patients with aneurysms on the basis of etiology was as follows: cardiovascular syphilis 9; arteriosclerosis 2. Among the 9 patients with cardiovascular syphilis there were several with multiple aneurysms, including 1 in the abdominal aorta (fig. 7). One of the arteriosclerotic aneurysms was a dissecting aneurysm and the other was saccular. Both were situated in the descending aorta.

Chronic pulmonary emphysema was characterized by right ventricular enlargement without generalized cardiac enlargement. In half of these cases we found the septum convex to the left, corroborating the findings of Sussman and his co-workers.[6] However, in some cases

Fig. 7.—*A*, slight obliquity with foreshortening of the left hemithorax showing multiple syphilitic aneurysms of the thoracic aorta. *B*, same as *A*, lateral view, showing aneurysm of the abdominal aorta.

similar deviations were observed in which there was right sided chamber enlargement and no emphysema.

In 1 instance we found enlargement in the hilar regions, which we thought were due to multiple aortic

6. Sussman, M. L.; Steinberg, M. F., and Grishman, Arthur: Contrast Visualization of the Heart and Great Vessels in Emphysema, Am. J. Roentgenol. **47**: 368-376 (March) 1942

aneurysms (fig. 10 *A*). Angiocardiography revealed large pulmonary arteries, the enlargements of which terminated quite abruptly.

Obstructions to the large vessels leading to the right side of the heart were easily visualized, as was the resulting secondary collateral circulation.

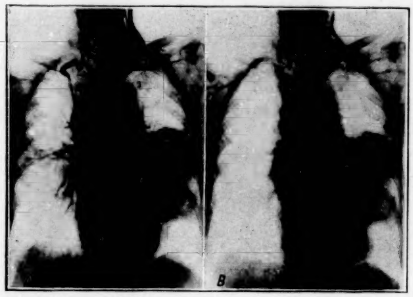

Fig. 8.—Arteriosclerotic aneurysm of the descending aorta of a white woman aged 93. Posteroanterior view showing the entire right side of the heart opacified. *B*, same as *A*, posteroanterior view, showing left side of the heart, aorta and aneurysm opacified.

In decided mediastinal deviations the size, shape and location of the heart and its chambers show significant variations from the normal. Intrinsic intrapulmonary obstructing factors existed which contributed to the changes observed. In 1 case in which the mediastinal structures were definitely deviated to the right (fig. 6 *A*) secondary to a pleural and pulmonary fibrosis with bronchiectasis, the evidence of obstruction was quite profound. The pulmonary vessels were extremely dilated, a dilatation carried all the way back to the heart, the superior vena cava, the subclavian and the axillary veins. An extensive collateral circulation was also demonstrable. Angiocardiography showed enlargement of the right and left chambers. The interventricular septum presented an accentuated convexity to the right. In the posteroanterior position, this septal convexity gave the right side of the heart a plow shaped appearance.

In a similar type case, but with the decided deviation of the heart to the left (fig. 6 *B*), the chambers assumed an entirely different shape. The right side of the heart was enlarged and the pulmonary vessels were extremely dilated. The U shaped structure appeared as a rectangle, with the upright portions of the U dilated and widely separated.

One patient presented typical clinical manifestations of bronchiectasis which could not be verified by bronchography. He was studied in order to determine the morphologic appearance of the parenchymal pulmonary arteries;[7] an obstructing lesion was suspected. Changes were observed, which we interpreted as a pulmonary endarteritis, with an extensive intrapulmonary collateral circulation. The large vessels showed a sudden reduction in the size of the lumens.

There were 4 cases presenting congenital cardiovascular anomalies. In 1, we were able to establish the diagnosis by direct evidence. In 3, the diagnosis was confirmed by indirect evidence.

In a case of dextra aorta the position of the aorta was demonstrated beyond any doubt (fig. 9).

In a case of coarctation, definite on clinical evidence, we were unable to demonstrate the constriction on three different occasions. On all examinations, the arch and descending portion of the aorta down to the level of the sixth thoracic vertebra were visualized with contrast substance with no sharp demarcation between the upper and lower portions of the descending aorta. Examinations were made at ten, eleven, twelve, fourteen, fifteen and sixteen seconds following injections, time factors which exceeded those determined by the circulation tests. Because of the constancy of the roentgen findings and despite the varying time factors, we concluded that the area of coarctation was at the level of the sixth thoracic vertebra.

In another instance a diagnosis of patent ductus arteriosus had been made clinically in a 12 year old boy. The right side of the heart was visualized in two and one-half seconds and the left side of the heart in seven seconds. The left pulmonary artery formed a prominence in the middle cardiac segment and contained contrast substance during both examinations. Under normal circumstances the left pulmonary artery should have been free of contrast substance at the end of seven seconds and should not have been opacified along with the left side of the heart and aorta. The inference was that the contrast substance had arrived in the left pulmonary artery by way of the aorta.

In the fourth case a white man aged 35 had a clinical diagnosis of pulmonary stenosis. At the end of three seconds (fig. 10 *B*) contrast substance was visualized simultaneously in the right and left ventricles, pulmonary aorta and pulmonary arteries. At the end of nine seconds contrast substance was present in the aorta and in the pulmonary arteries. The presence of contrast substance in both ventricles at three seconds could be accounted for only by an interventricular septal defect. Persistence of contrast substance in the large pulmonary vessels was further evidence of a septal defect.

The hypertensive type heart showed cardiac hypertrophy, as was to be expected. In some instances the

Fig. 9.—*A*, posteroanterior view showing the left side of the heart and aorta opacified and aorta to the right of the spine. *B*, left anterior oblique view. The left side of the heart is opacified, showing loss of normal aortic curve, resembling that observed in the right anterior oblique view.

hypertrophy reached enormous proportions, not only of the left ventricular wall but of the right as well. In others there was an accompanying enlargement of the left ventricular chamber (fig. 5).

The arteriosclerotic hearts showed no true cardiac enlargement or hypertrophy but showed enlargement of

7. Brill, I. C., and Krygier, J. J.: Primary Pulmonary Vascular Sclerosis, Arch. Int. Med. **68**: 560-577 (Sept.) 1940.

the right heart chamber.[8] More often, the inverted mushroom type of enlargement of the right side of the heart was found in these cases.

As the right side of the heart enlarges, it appears, in the left anterior oblique position, as if the right ventricular apex were elevated and directed posteriorly, giving the impression that there might be a counterclockwise or posterior rotation of the heart on a horizontal axis.

The rheumatic hearts frequently showed evidence of cardiac enlargement. This increase in size was due in some to enlargement of the chamber, in others to hypertrophy and in still others to a combination of the two conditions.

Enlargement of the right side of the heart did not present the appearance of an inverted mushroom in the left anterior oblique position. As the right side of the heart enlarges, the structures to the left of the base of the right ventricle may be displaced to the left and produce the convexity in the middle cardiac segment.

At times the typical configuration ascribed to mitral hearts was noted. Often there was an associated enlargement of the right heart chamber with little or no evidence of hypertrophy. Some showed increase in the transverse diameter of the horizontal portion of the U between the right auricle and the right ventricle. A loss of demarcation between the left ventricle and the aorta we attributed to valvular insufficiency.

Those patients with clinical mitral stenosis showed large left auricles. In the posteroanterior view the enlarged left auricle was disposed to the right and did not contribute to the formation of the left border of the cardiac silhouette. However, when the left auricle is very large it forms part of the right border of the cardiac silhouette.

We have been unable to demonstrate the left auricle on the left border, just as we have been unable to demonstrate the conus as forming the convexity of the middle cardiac segment. We believe that as the left auricle enlarges and rotates posteriorly to appear on the right cardiac border structures lying to its left lateral border are pushed and form the convexity seen in mitral stenosis. The structure called "conus" on the roentgenogram is not the anatomic conus. The anatomic conus is an intracardiac and not contour forming structure. We have found the convexity to be formed by the left pulmonary artery as it assumes an oblique intracardiac downward course instead of the usual horizontal.

SUMMARY

1. A total of two hundred and fifteen injections were made with 70 per cent diodrast solution in a series of 100 persons, ranging in age from 12 to 93 years, in order to visualize the cardiac chambers and the large vessels. Included in this group were persons with and without cardiovascular disease.

2. Reactions to the injections were observed in most persons, but no reaction was severe enough to warrant discontinuing the examination, and no patient objected to a second injection. The chief reaction was a sharp transient drop in the blood pressure.

3. This study yielded information of an anatomic nature of the heart and blood vessels, information at variance with the ordinarily accepted concept of the normal heart. In contrast to our past concept concerning the anatomic positions of the cardiac chambers and the great vessels, the following points were determined:

A. There is a deep location of the ventricular conus.

B. Pulmonary aorta as it arises from the ventricle is situated deep in the cardiac silhouette and does not form a prominence on the left border of the heart.

C. That portion of the cardiac silhouette above the base of the left ventricle and below the left pulmonary artery is usually not opacified with contrast substance and must indicate an area that is not hollow but solid.

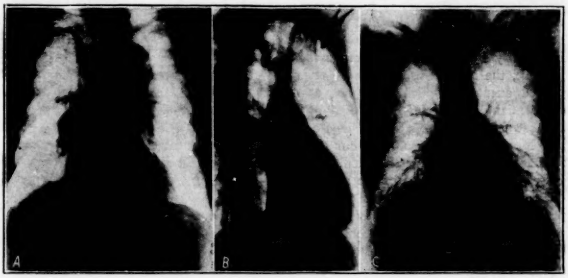

Fig. 10.—*A*, posteroanterior view showing very large pulmonary arteries without any clinical evidence of parenchymal obstruction. *B*, right anterior oblique view showing the superior vena cava, right and left ventricle and pulmonary arteries opacified in three seconds. *C*, posteroanterior view showing pulmonary endarteritis with extensive intrapulmonary collateral circulation.

In our series, there was one exception, and we thought it was the presence of a left auricular appendage.

D. The middle cardiac segment of the left border of the heart is formed by the pulmonary aorta and the left pulmonary artery.

E. The nonopacified portion of the lower right cardiac border is the inferior vena cava.

F. The right heart does not occupy the major portion of the cardiac silhouette in the posteroanterior projection. The left ventricle occupies a considerable portion of the cardiac silhouette instead of, as previously supposed, only a small strip along the left cardiac silhouette.

4. The following were demonstrated by angiocardiography:

A. Chamber enlargement.
B. Muscular hypertrophy.
C. Stenotic lesions.
D. Regurgitant lesions.
E. Congenital anomalies by both direct and indirect evidence.
F. Aneurysm of the thoracic and abdominal aorta (differentiation of mediastinal lesions from vascular lesions).
G. Obstructive lesions of superior vena cava and outline of the collateral circulation.
H. Alterations in the pulmonary parenchymal circulation.

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8. By arteriosclerotic hearts we mean hearts in persons with no antecedent history of essential hypertension or myocardial infarction, whose blood pressure does not exceed 150 in the systolic level or 90 in the diastolic, who have definite evidence of peripheral sclerosis and who are 45 years of age or over. They may have an anginal syndrome and/or electrocardiographic evidence of myocardial damage.

ABSTRACT OF DISCUSSION

DR. M. F. STEINBERG, New York: The development of contrast roentgenography of the cardiovascular system has stimulated the clinician and the roentgenologist to a clearer understanding of fundamental cardiovascular problems. Angiocardiography and arteriography have opened diagnostic vistas hitherto unattainable, and these may prove as rich as those resulting from the development of cholecystography, urography and encephalography. The application of this technic allows the most intimate study of circulatory anatomy and dynamics. The position of the pulmonic conus and the supravalvular portion of the aorta has been demonstrated within the cardiac shadow. The interventricular septum has been delineated and its position ascertained directly. A word of caution must be given concerning the value of measurements of the myocardial walls and the size of the chamber cavities. In serial exposures these have been found to vary greatly during systole and diastole. For the present it would be wiser to refrain from such measurements until one can be assured of synchronous exposures either in systole or in diastole. The value of angiocardiography in the differential diagnosis of mediastinal masses is indisputable. At the Mount Sinai Hospital all circumscribed mediastinal masses in the region of the vascular pedicle are studied preoperatively by this method in order to differentiate, as far as possible, the aneurysms. We have encountered 2 instances of proved aneurysm which were not opacified. Hence, in the differential diagnosis of mediastinal masses, angiocardiography is most significant when the findings are positive. Drs. Taylor and McGovern have confirmed our observations on the change in the position of the interventricular septum in cases of chronic lung disease. Convexity of the septum to the left occurred in 43 per cent of our series of 28 cases of emphysema, asthenia, pulmonary fibrosis and bronchiectasis. However, in most of the cases which did not show this change we found some factor causing left ventricular strain, either hypertension or coronary artery disease. The most practical application of the value of angiocardiography in congenital heart disease has been found in confirmation of the clinical diagnosis of patent ductus arteriosus. Dilatation of the pulmonary artery or its branches is not pathognomonic nor is it a constant feature. We place great diagnostic importance, however, on the finding of a peculiar dilatation in the descending aorta just beyond the origin of the subclavian artery. This has been seen in no other condition than patent ductus arteriosus and was found in 26 of 27 cases. We believe that it represents either the infundibulum of the ductus or a traction aneurysm of the descending aorta due to the "pulling" effect of the short ductus.

DR. MERRILL C. SOSMAN, Boston: I feel that we have gained considerable useful knowledge by the contrast cardiography, but this is still a highly specialized procedure and we must expect the men who are trained and equipped to do it to supply us with these new criteria so that we can interpret them or can use them in our interpretations of the films we get by ordinary means. I think probably the most valuable result of this work is the stimulation of a renewed interest in cardioroentgenology.

DR. HENRY K. TAYLOR, New York: The questions propounded by Dr. Sosman are very pertinent. Unusual procedures are attempted only after all other methods have been tried; the deciding factor is always How much will the patient benefit by them from either the diagnostic or the therapeutic standpoint?

The Heritage of Courage and Kindness.—The most effective teacher is not the colorless intellectual virtuoso who today deals out as a fact what tomorrow may prove to be only a fancy, or who pursues some petty experimental project; but he is the real doctor who transmits to his pupils the heritage of truth, courage, and kindness that will make his spiritual heirs worthy members of the medical profession.—Irving, Frederick C.: Safe Deliverance, Boston, Houghton Mifflin Company, 1942.

THE FUNCTIONAL VALUE OF THE LIVER IN HEART DISEASE

AN EXPERIMENTAL STUDY

PROF. DR. IGNACIO CHÁVEZ
DR. B. SEPÚLVEDA
AND
DR. A. ORTEGA I.
MEXICO CITY

One of the organs that suffers most in heart failure is undoubtedly the liver. Its enlargement is the general rule in right congestive heart failure as well as in total ventricular failure. But if it is easy to appreciate the anatomic alterations—enlargement, tenderness, hardness and the like—the functional attack often passes unnoticed or at least is clinically underestimated. It is only in the advanced stages when subicterus, or rarely icterus, appears or when digestive disturbances become important that the physician directs his attention toward the liver and admits the existence of hepatic insufficiency. Nevertheless, at much earlier stages of congestion laboratory procedures already show the functional attack of the gland.

TABLE 1.—*Classification of Cardiac Patients*

	With Decompensation	Without Decompensation
Rheumatic heart disease	19	3
Syphilitic aortitis	3	2
Arteriosclerotic heart disease	5	0
Miscellaneous group (congenital, cor pulmonale and thyrotoxic heart)	3	0
	30	5

It is conceivable that this hepatic involvement should be practically inevitable in heart failure, even in its early stages, as a result of a combination of factors: first, the engorgement of the organ with its consequent effects on the nutrition of the hepatic cell; second, general anoxemia resulting from a defective pulmonary circulation; and, third, the possibility of an aggressive action of the cause of the heart disease itself—rheumatism, syphilis and like conditions.

In the face of scarcity of the usual clinical data, as well as the tardiness with which they appear; in view of the importance of a better knowledge of the functional capacity of the liver in our cardiac patients, and with the desire of learning whether or not the fourth factor mentioned, i. e. the aggressive action of the underlying cause of the heart disease, adds its part to the clinical picture of the congested liver, we have subjected a group of our cardiac patients to a certain number of experimental tests.

This particular chapter dealing with the functional exploration of the liver is one of the most debated in medicine. The literature on the subject is extensive without there being, at present, complete agreement as to the value of the test proposed.

This lack of uniformity in criterion is explained by various reasons: 1. The liver has a multiplicity of

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functions some of which are so poorly understood that they cannot be correctly explored. 2. Under pathologic conditions not all functions are affected at the same time or to the same degree—what has been called "functional asynergy" by Fiessinger and Walter. 3. The functional capacity of the organ varies constantly; the liver is a dynamic, not a static, gland, as Mann expresses it. 4. The liver has a great regenerative power and normally does not work at its full capacity. For the functional tests to give positive results an extensive attack of the gland carried to a more or less intensive degree is necessary.

These considerations of a physiologic nature, accurate as they are, do not invalidate the use of the tests; they only indicate certain conditions for their execution and fix certain limits as to the value of the results obtained. The following are the practical consequences that one may deduce from them: (*a*) It is necessary to perform several tests at the same time for the purpose of simultaneously exploring the greatest possible number of functions: it is the so-called "hepatic snapshot" of Fiessinger. (*b*) It is imperative to repeat the tests in order to obtain an idea of the evolution which the functions undergo in the course of time. (*c*) The results of the tests should always be confronted with clinical data.

Investigations that have filled these requirements and that have been carried out on cardiac patients are not very numerous as far as we have been able to determine. In 1930 Jolliffe [1] published a study on functional tests carried out on 16 patients with heart failure; in 1932 Robertson, Swalm and Konzelmann [2] reported the results obtained on 15 patients, most of whom were suffering from heart failure; in 1935 Routier, Cottet and Molinghen [3] explored the livers of 35 cardiac patients by means of several simultaneous tests. Later on we shall compare the conclusions of these authors with our own.

CASES STUDIED

In the present research 35 patients with heart disease from various causes were studied, 30 of whom had heart failure and 5 had no insufficiency. Six of those with heart failure were examined for the second time after a disappearance of, or at least an improvement in, their insufficiency, which raises the number of observations to 41. Finally, 4 patients with liver disease were studied as a control group in order to check the results of the tests.

One group of cardiac patients was divided as shown in table 1.

For the convenient appreciation of the results, we have diagrammatically classified the heart failure of our patients into four degrees: 1, slight; 2, medium; 3, accentuated; 4, extreme.

The heart failure of all our patients was congestive. The enlargement of the liver was estimated according to the number of centimeters which it measured below the costal arch at the mammary line.

The patients were subjected to a careful clinical study as well as to roentgen examination, an electrocardiographic study, a previous urinalysis, chemical analysis of the blood, blood counts, a Bordet Wassermann test, determination of the sedimentation rate, and like laboratory examinations.

1. Jolliffe, Norman: J. Clin. Investigation **8**: 419-433 (April) 1930.
2. Robertson, W. E.; Swalm, W. A., and Konzelmann, F. W.: Functional Capacity of the Liver: Comparative Merits of the Most Popular Tests, J. A. M. A. **99**: 2071-2077 (Dec. 17) 1932.
3. Routier, D.; Cottet, J., and Molinghen, P.: Arch. d. mal. de l'app. digestif **25**: 801 (Oct.) 1935.

TESTS EMPLOYED

The tests conducted by us were:

1. Investigation of bile pigments in the serum: van den Bergh's reaction.
2. Measurement of urobilinogen in a specimen of urine.
3. Rosenthal's test with bromsulphalein.
4. The Takata-Ara reaction.
5. The induced galactosuria test.

BILIRUBINEMIA

For serum bilirubin determination we have followed Jendrassik's technic and have used Summerson's photoelectric colorimeter. We conducted first the ring test

TABLE 2.—*Bilirubin*

	Case	Grade	Direct	Bilirubin: Indirect, Mg./100 Cc.	Bilirubin: Total, Mg./100 Cc.
First Group: Rheumatic Endomyocarditis—24 Cases					
Without cardiac failure (4 cases)	25	..	—	0.25	....
	8	..	—	0.48	....
	1	..	—	0.25	....
	12 bis	..	—	0.50	....
With cardiac failure (20 cases)	23 bis	1	—	0.40	....
	3	1	—	0.37	....
	30	1	—	0.75	....
	27 bis	2	+	0.45	....
	31	2	+	....	0.50
	14	2	+	....	0.55
	11	2	+	....	1.50
	2	2	+	....	0.85
	22	2	+	....	1.00
	29	3	+	....	1.50
	23	3	+	....	1.50
	21	3	+	....	1.40
	12	3	+	....	1.86
	16	3	—	0.50	....
	27	3	+	0.90	....
	5	3	+	....	2.92
	18	4	+ 1.22	0.90	2.12
	28	4	+ 5.00	1.90	6.90
	4	4	+	....	1.36
	39	4	+	....	4.98
Second Group: Syphilitic Aortitis—6 Cases					
Without cardiac failure (2 cases)	9	..	—	0.25	....
	26	..	—	0.50	....
With cardiac failure (4 cases)	32 bis	1	+	....	0.25
	32	3	+	....	0.80
	33	3	+	....	0.60
	6	4	+	....	2.00
Third Group: Cardioangiosclerosis—6 Cases					
All in cardiac failure	17	1	+	....	1.73
	15	2	+	....	1.07
	10	2	—	0.25	....
	13 bis*	2	+	....	1.65
	13	3	+	....	2.25
	19	3	+	....	1.50
Fourth Group: Miscellaneous—3 Cases					
Congenital heart disease, septal communication, cardiac failure	7	3	+	....	3.00
Cor pulmonale (cardiac failure)	24	2	+	....	0.80
Thyrotoxicosis (cardiac failure)	20	2	+	....	1.50

* This patient had besides an alcoholic and syphilitic hepatitis.

of Lepehne to determine qualitatively whether or not direct bilirubin was present, either immediate or delayed in its appearance. If it was negative, we proceeded with the quantitative determination of indirect bilirubin, following the method of Jendrassik and Czike. If it was positive and the ring of Lepehne revealed a weak reaction, we were satisfied with labeling it as such, without attempting the measurement, since the results obtained are always inexact if not misleading. In case of an intensively positive reaction, we proceeded to the separate determination of both bilirubins by the aforementioned method of Jendrassik and Czike.

We accept as normal for indirect bilirubin 0.1 to 0.5 mg. per hundred cubic centimeters of blood. This figure, determined by Barrón [9] using van den Bergh's reaction, is in accordance with our own experience.

9. Barrón, E. S. G.: Medicine **10**: 77-133 (Feb.) 1931.

We have considered as abnormal the presence of bilirubin in the following conditions: (*a*) when indirect bilirubin is greater than 0.5 mg. per hundred cubic centimeters, (*b*) when direct bilirubin is present, whatever its amount, and (*c*), as is obvious, when total bilirubin is increased at the expense of its two fractions.

Of the 16 patients with heart failure studied by Jolliffe, 81 per cent showed an elevation of the blood bilirubin. On the other hand, in 14 cardiac patients, some with insufficiency and others without, studied by Robertson, Swalm and Konzelmann,[2] not a single direct van den Bergh reaction was found, and as for the indirect they found it normal in the majority of cases, from which they concluded that this reaction is of little importance in the study of cardiac patients.

TABLE 3.—*Bromsulphalein*

	Case	Grade	Retention, per Cent
First Group: Rheumatic Endomyocarditis—24 Cases			
Without cardiac failure (4 cases).....	8*	..	Negative
	1	..	6
	12 bis	..	10
	25	..	12
With cardiac failure (20 cases).....	33 bis	1	20
	22 bis	1	39
	30	1	18
	31	2	14
	14	2	22
	11	2	20
	2	2	40
	22	2	40
	27 bis	2	40
	29	3	64
	32	3	48
	21	3	42
	12	3	28
	16	3	14
	27	3	60
	18	4	40
	28	4	60
	4	4	14
	39	4	72
	5	3	62
Second Group: Syphilitic Aortitis—6 Cases			
Without cardiac failure (2 cases).....	9	..	Negative
	26	..	12
With cardiac failure (4 cases).....	32 bis	1	12
	32	3	30
	33	3	28
	6	4	36
Third Group: Cardioangiosclerosis—6 Cases			
All in cardiac failure.....	17	1	28
	15	2	34
	10	2	15
	13	3	48
	19	3	34
	13 bis †	2	64
Fourth Group: Miscellaneous—2 Cases			
Congenital heart disease, septal communication, cardiac failure.....	7	3	78
Thyrotoxicosis, cardiac failure.....	20	2	34

* This patient just recovered from cardiac failure.
† This patient had besides an alcoholic and syphilitic hepatitis.

Inversely, Routier, Cottet and Molinghen [3] affirm that in 31 patients with heart failure seen by them indirect bilirubin was always increased, and the direct was positive in only 2 cases.

Our Results.—In the present study, which includes 33 tests carried out on 30 cardiac patients with varying degrees of heart failure (1 to 4), bilirubin was abnormal in 28, or 85 per cent. On the other hand, of 6 cardiac patients who had no decompensation, all had normal bilirubin. It is worthy of note that patient 12 bis had previously had during his course of heart failure a positive direct bilirubin reaction and a total bilirubin of 1.86 per cent. Another patient, 23 bis, with normal reactions, had also shown a few days before, during a grade 3 insufficiency, direct positive bilirubin and a total bilirubin of 1.50 per cent.

In table 2 it can be observed that:

1. In the group of patients with heart failure, even if the failure was not constant, there existed a close relation between the degree of failure and the amount of bilirubin; in the group with slight failures (type 1), in which there were 4, only 1 had a positive direct reaction and that was a patient with long-standing syphilis with aortitis. In the other 3, indirect bilirubin remained normal or hardly superseded the normal limit. In the group with failures of class 2, which included 13 patients, all presented direct bilirubin, and the total bilirubin, with the exception of 3 in whom it remained normal, reached figures which ranged between 0.5 and 1.7 mg.; in the group with advanced failures (type 3), which included 11 patients, all with 1 exception had direct bilirubin and total figures which reached 2.25 and 3 mg.; finally in the group with grade 4 failures, which included 5 patients, all had direct bilirubin, and total figures were high, from 1.36 to 6.9 mg. per hundred cubic centimeters.

2. In this table it can be appreciated that there is no striking significant relationship between the cause of cardiac disease and the degree of bilirubinemia; still the impression is gained that it is in the group of patients with rheumatic heart disease that the highest figures of bilirubin are to be found.

3. Finally, it was not possible to appreciate a fixed, stable relation between the degree of liver enlargement and the amount of bilirubin. Generally speaking, the livers with the greatest amount of enlargement are those with the most pigment; but the exceptions are numerous, as in case 33 bis, in which the liver measured 3 cm. beyond the costal arch, and in case 16, in which the liver measured 8 cm. and the bilirubin was normal, while in others in which there was less enlargement of the liver very high figures were obtained.

BROMSULPHALEIN TEST

Since the studies of Rosenthal and White,[11] bromsulphalein has been the dye of choice used for studying elimination by the liver. The dose of 5 mg. per kilogram of body weight which we used is the one recommended by O'Leary, Greene and Rowntree.[12]

There are cases in which the test is not applicable, as in frank jaundice; on the other hand, if the amount of bilirubin is moderate the test retains all its usefulness. Snell and Magath,[13] after a survey of more than 10,000 tests of this kind performed in the Mayo Clinic, have concluded that bromsulphalein does permit one to judge the condition of the liver if bilirubin does not exceed 5 mg., and they even consider that it is perhaps the best functional test available at present.

In accordance with our experience, we have considered as abnormal all retentions of the dye which are greater than 10 per cent thirty minutes after the injection. Retentions of this type were considered positive.

Jolliffe, in the study already mentioned, using Rosenthal's original technic of an injection of 2 mg. per kilogram of body weight, found retentions ranging from 5 to 20 per cent in 75 per cent of his cases. Robertson, Swalm and Konzelmann,[2] with doses of 5 mg. per kilogram, found in all of their 9 cases retentions greater than 6 per cent.

11. Rosenthal, S. M.: J. Pharmacol. & Exper. Therap. **19:** 385-391 (June) 1922. Rosenthal, S. M., and White, E. C., ibid. **24:** 265-284 (Nov.) 1924; Clinical Application of Bromsulphalein Test for Hepatic Function, J. A. M. A. **84:** 1112-1114 (April 11) 1925.
12. O'Leary, P. A.; Greene, C. H., and Rowntree, L. G.: Clinical Evaluation of Galactose Tolerance Test, Arch. Int. Med. **44:** 155-193 (Aug.) 1929.
13. Snell, A. M., and Magath, T. B.: Use and Interpretation of Tests for Liver Function, J. A. M. A. **110:** 167-174 (Jan. 15) 1938.

Our Results.—We carried out 38 tests on our 35 patients, 6 tests on patients without heart failure and 32 on patients with varying degrees of decompensation including various factors. Among those cases without failure the reactions in only 3 were negative; in the other 3 moderate retention rates, from 10 to 12 per cent, were present.

In the 32 cases presenting heart failure, which are classified in table 3, we obtained the following results:

Five patients with heart failure grade 1: all gave a positive reaction, with retentions ranging between 12 and 30 per cent and averaging 21 per cent.

Ten patients with heart failure grade 2: all gave a positive reaction, with retentions ranging between 14 and 40 per cent and averaging 28.8 per cent.

Twelve patients with heart failure grade 3: all gave a positive reaction, with retentions ranging from 14 to 78 per cent and averaging 43 per cent.

Five patients with heart failure grade 4: all gave a positive reaction, with retentions ranging between 14 to 72 per cent and averaging 44.4 per cent.

It is of interest to note in table 3 that among those patients studied twice, once during heart failure and again after they had improved or been relieved of it, the retention of the dye decreased or disappeared; as in case 12, in which on the first test there was a retention of 28 per cent and after relief it went down to 10 per cent, and in cases 23, 22 and 32, presenting retentions of 48, 40 and 30 per cent respectively, in which on improvement the rates were lowered to 20, 30 and 12 per cent respectively.

THE TAKATA-ARA TEST

The Takata-Ara reaction, which when applied to the functional study of the liver should in all justice be termed the Takata-Jezler reaction, has been studied by numerous investigators but to date there is no uniformity of opinion with regard to its diagnostic or its prognostic value or even as to its technic, much less as to the explanation of its mechanism. Magath [14] has recently made a revision of the subject, as has Naville in France.[15] It is accepted that at present this reaction is entirely empirical and that it is most probable that it stands in relation with the absolute and relative amounts of albumin and globulin in the serum, since its greatest occurrence is in connection with alterations of the blood proteins. Nevertheless it seems that the liver takes a direct part in the formation and regulation of these plasma proteins. The experiments of Jürgens appear to bear this out. This investigator has been able to modify the production of the serum proteins in the dog and goose by ligating the portal vein and by means of Eck's fistula. In these cases the reaction of Takata-Ara becomes positive but again becomes negative if the liver of the animal under experimentation is removed.

Fully aware that it lacks specificity and that there are extrahepatic factors which influence the proportion of serum proteins, such as feeding, conditions of the kidney, thyroid activity and the like, we have included the Takata-Ara-Jezler reaction in the present study, more in the hope of gathering information on the subject than because of any idea on our part that it is a true test of hepatic function.

The results of the test have been different and even contradictory in the hands of diverse authors. Girard and Vincent [16] have found negaitve reactions in all their cases of cardiorenal disease complicated with heart failure. Crane [17] obtained the same negative results in 3 cases of cardiac hypertension. On the other hand, Horejsi [18] found a positive reaction of 37 per cent in 10 cardiac patients. Jezler, quoted by Wayburn and Cherry,[19] reports 28 positive reactions among 218 patients with decompensation, or a rate of 13 per cent. Wayburn and Cherry, studying 122 cases of that type of disease, found only 9 positive reactions, or 7.4 per cent, and in a survey of the literature they collected 453 case reports published by eight different investigators

TABLE 4.—*Takata-Ara Test*

	Case	Grade	Result
First Group: Rheumatic Endomyocarditis—24 Cases			
Without cardiac failure (4 cases).....	25	..	—
	8	..	—
	1	..	—
	12 bis	..	++
With cardiac failure (20 cases).....	23 bis	1	—
	3	1	—
	30	1	—
	27 bis	2	+++
	31	2	—
	14	2	++
	11	2	++
	2	2	++
	22	2	++
	29	3	+++
	23	3	+++
	21	3	+++
	12	3	+
	27	3	+++
	16	3	—
	5	3	+++
	18	4	++
	28	4	+++
	4	4	—
	39	4	+++
Second Group: Syphilitic Aortitis—6 Cases			
Without cardiac failure (2 cases).....	9	..	—
	26	..	—
With cardiac failure (4 cases).....	32 bis	1	—
	32	3	—
	33	3	—
	6	4	++
Third Group: Cardioangiosclerosis—6 Cases			
All in cardiac failure.....	17	1	+
	15	2	+
	10	2	++
	13 bis	2	—
	18	3	++
	19	3	++
Fourth Group: Miscellaneous—3 Cases			
Septal communication (cardiac failure).....	7	3	—
Cor pulmonale (cardiac failure).....	24	2	—
Thyrotoxicosis (cardiac failure).....	30	2	++

(themselves included). In this group there were 60 with a positive reaction, or 13.3 per cent, a rate which might at present serve as a standard by which to judge the frequency of the reaction in the course of heart failure.

Our Results.—In 30 cases of heart failure studied by us, of different causes and of different degrees, as specified in table 4, we found the Takata-Ara reaction positive in 19, or in 63.3 per cent. On the contrary, 7 cardiac patients without heart failure all had, with 1 exception, a negative reaction.

At a glance it can be appreciated that (1) the reaction is devoid of all specificity, for even though it is negative in all except 1 of the cases without heart failure it is also negative in all except 1 of the cases with slight heart failure and in several of those with

14. Magath, T. B.: J. Lab. & Clin. Med. **26:** 156-173 (Oct.) 1940.
15. Naville M.: Ann. de méd. **40:** 28 (June) 1936.
16. Girard, M., and Vincent, D.: Lyon méd. **160:** 672 (Dec.) 1937.
17. Crane, M. P.: Am. J. M. Sc. **187:** 705-710 (May) 1934.
18. Horejsi, J.: Acta med. Scandinav. **96:** 408-421, 1938.
19. Wayburn, E., and Cherry, C. B.: Am. J. Digest. Dis. **5:** 231-238 (June) 1938.

advanced failure, and (2) the intensity of the reaction does not run parallel with the degree of heart failure or with the size of the liver, and it is not influenced by the underlying cause of heart disease.

Comments.—The unsuspected frequency of 63.3 per cent at which we found it to be positive, and which is a very much higher rate than the usual average of 13.3 per cent, does not fail to surprise us considerably. The only explanation that we can offer is that in the group of patients with advanced heart failure, subjected over long periods of time to dietary deficiencies, their hypoproteinemia is so advanced that it complicated a situation which is of itself highly chronic in undernourished persons with low protein intake, as frequently occurs among the poor people of our charity wards. Nevertheless it is well to note that we did not find any correlation whatever between the intensity of the Takata-Ara reaction and the degree of anemia or with the time of evolution of the disease or of the heart failure.

TABLE 5.—*Urinary Urobilinogen*

	Case	Grade	Urobilinogen, Mg.	Van den Bergh Units
First Group: Rheumatic Endomyocarditis—14 Cases				
Without cardiac failure (3 cases)...	8	..	0.20	0.40
	1	..	0.50	1.00
	12 bis	..	0.30	0.60
With cardiac failure (11 cases).....	3	1	0.77	1.53
	27 bis	2	0.25	....
	14	2	0.37	0.75
	11	2	2.00	4.00
	2	2	2.50	5.00
	29	3	2.00	4.00
	12	3	1.00	2.00
	27	3	0.63	1.26
	28	4	1.00	2.00
	4	4	3.88	7.75
	5	3	6.20	12.40
Second Group: Syphilitic Aortitis—4 Cases				
Without cardiac failure (1 case)....	9	..	0.17	0.33
With cardiac failure (3 cases).....	32 bis	1	0.25	0.50
	33	3	0.75	1.50
	32	3	1.00	....
Third Group: Cardioangiosclerosis—3 Cases				
All in cardiac failure.....	15	2	0.70	1.40
	10	2	0.25	0.50
	13	3	1.25	2.50
Fourth Group: Miscellaneous—1 Case				
Congenital heart disease, septal communication, cardiac failure...	7	3	1.00	2.00

TABLE 6.—*Examples of Determination of Concentration of Galactose*

	Urine, Cc.	Galactose, Gm.	Concentration per Thousand
Normal case			
Sample 1.....	250	1.2	4.8
Sample 2.....	200	0.2	1
Sample 3.....	600	0.0	...
Sample 4.....	700	0.0	...
Pathologic case			
Sample 1.....	100	2.0	20
Sample 2.....	250	3.5	14
Sample 3.....	400	1.5	3.75
Sample 4.....	500	1.0	2

UROBILINOGEN

According to the technic proposed by Watson,[23] normal figures for urobilinogen in the twenty-four hours of the day vary between 0 and 4 mg., the most frequent being between 0.5 and 2 mg. a day. Notwithstanding that this procedure is extremely accurate, we were not able to adopt it because of technical difficulties. It would have been necessary to collect the urine of twenty-four hours, in addition to collecting the urine employed in the galactose test, also for twenty-four hours, all of which would have lengthened the process so much as to deprive it of its "snapshot" quality and at the same time would have postponed treatment of cardiac patients who were not in a condition to withstand a very long delay.

Consequently we selected Scott's technic, which also measures urobilinogen but requires only 1 specimen of freshly voided urine. It is true that the method can be criticized on the ground that urobilinogen is not uniformly eliminated in the twenty-four hours, but, since this varies within very short limits and Scott's method has the obvious advantages of simplicity and exactness, we adopted it as the method which seemed to suit our purposes exactly.

The normal amount of urobilinogen in fresh urine varies between 0.1 and 0.25 mg. per hundred cubic centimeters, according to the figures given by Scott; but we call attention to the fact that in a considerable number of normal subjects it is not infrequent to find figures below the 0.1 mg. which we have just pointed out as a normal minimum.

TABLE 8.—*Induced Galactosuria*

	Case	Grade	Thiebaut	Bauer
First Group: Rheumatic Endomyocarditis—8 Cases				
Without cardiac failure (1 case)....	25	..	Positive	Negative
With cardiac failure (7 cases).....	23 bis	1	Positive	Negative
	27 bis	2	Negative	.....
	31	2	Positive	Negative
	22	2	Positive	Positive
	29	3	Positive	Negative
	27	3	Positive	.....
	28	4	Positive	Negative
Second Group: Syphilitic Aortitis—5 Cases				
Without cardiac failure (2 cases)...	9	..	Positive	Not done
	26	..	Positive	Negative
With cardiac failure (3 cases).....	32 bis	1	Positive	Negative
	32	3	Positive	Negative
	33	3	Positive	Negative
Third Group: Cardioangiosclerosis—2 Cases				
Both in cardiac failure.....	15	2	Positive	Not done
	10*	2	Negative	Not done
Fourth Group: Miscellaneous—2 Cases				
Cor pulmonale (cardiac failure)....	24	2	Positive	Negative
Septal communication (cardiac failure).....	7	3	Positive	Not done

* This patient also showed renal insufficiency, which accounts for the absence of galactose elimination.

Jolliffe [1] has found urobilinogen increased in more than half of his 16 cases (56 per cent). On the other hand, Robertson, Swalm and Konzelmann have found it normal in practically all their patients. Watson [22] finds the rates elevated in 9 of the 11 patients studied by him (81 per cent).

Our Results.—In our study we carried out the measurement of urobilinogen in 18 cardiac patients with heart failure and in 3 without it, as is shown in table 5, in which it can be seen that:

1. In the small group of cardiac patients without heart failure not 1 had an increase in urobilinogen.

2. In the group of 18 patients with heart failure, only 5 maintained normal rates, and all were only moderately decompensated; the remaining 13, or 75 per cent, had high rates, but there was no significant correlation between these rates and the degree of failure.

3. Nevertheless, it could be observed that in 2 of them (cases 12 and 27), on improvement of their condition, the urobilinogen rates returned to normal.

23. Watson, C. J.: Am. J. Clin. Path. **6**: 458-475 (Sept.) 1936.

4. Even though the number of observations is too small to permit us to generalize, it seems that in equal stages of failure the group of rheumatic patients presents higher urobilinogen rates than the other groups.

5. There is no constant relation between the size of the liver and the degree of reaction.

THE INDUCED GALACTOSURIA TEST

The original technic of Bauer consists in the oral administration of 40 Gm. of galactose apart from meals and measurement of the amount of sugar in the urine five hours later. An elimination greater than 3 Gm. is considered pathologic.

Our Results.—For the purposes of our study we began the test in 27 cases but were able to complete it in only 17. The other 10 were not taken into account because of the impossibility of obtaining one or more samples of urine at the required time. This fact was due to the presence of great oliguria, and we were therefore unable to correct it; even the catheter was useless in cases in which the urinary bladder was empty. This circumstance, and the great frequency with which it repeated itself—in one third of the cases—constitute a serious inconvenience in the use of the test for cardiac patients.

TABLE 9.—*Comparative Results of Bromsulphalein Test, Blood Bilirubin and Urinary Urobilinogen*

	Case	Grade	Liver, Cm. Below Costal Margin at Mammary Line	Bromsulphalein, Retention, per Cent	Blood Bilirubin			Urobilinogen, Mg./100 Cc.
					Direct, Mg./100 Cc.	Indirect, Mg./100 Cc.	Total, Mg./100 Cc.	
Without cardiac failure	8	..	Normal size	Negative	—	0.48	....	0.20
	1	..	Normal size	6	—	0.25	....	0.55
	12 bis	..	Normal size	10	—	0.50	....	0.30
	25 bis	..	Normal size	12	—	0.25	....	....
With cardiac failure	23 bis	3	1	20	—	0.40	....	....
	30	1	2	18	—	0.75	....	....
	27 bis	2	Normal size	40	+	0.45	....	0.25
	31	2	4	14	+	....	0.50	....
	14	2	Normal size	22	+	....	0.35	0.37
First Group: Rheumatic Endomyocarditis								
	11	2	6	20	+	....	1.50	2.00
	2	2	3	40	+	....	0.85	2.50
	22	2	6	40	+	....	1.00	....
	29	3	8	64	+	....	1.50	2.00
	23	3	6	48	+	....	1.50	....
	21	3	9	42	+	....	1.40	....
	12	3	8	28	+	....	1.86	1.00
	16	3	8	14	—	0.50	....	....
	27	3	4	60	+	0.90	....	0.63
	18	4	6	40	+ 1.22	0.90	2.12	....
	28	4	6	60	+ 5.00	1.90	6.90	1.00
	4	4	7	14	+	....	1.36	3.88
	39	4	Normal size	72	+	....	4.98	....
	5	3	Normal size	62	+	....	2.92	6.20
Second Group: Syphilitic Aortitis								
Without cardiac failure	9	..	.....	Negative	—	0.25	....	0.17
	26	..	.....	12	—	0.50	....	....
With cardiac failure	32 bis	1	Normal size	12	+	....	0.25	0.25
	32	3	4	30	+	....	0.80	....
	33	3	4	28	+	....	0.60	0.75
	6	4	Normal size	36	+	....	2.00	....
Third Group: Cardioangiosclerosis								
All in cardiac failure	17	1	5	28	+	....	1.73	....
	15	2	2	34	+	....	1.07	1.00
	10	2	4	15	—	0.25	....	0.50
	13 bis	2	12	64	+	....	1.65	....
	13	3	8	48	+	....	2.25	1.25
	19	3	4	34	+	....	1.50	....
Fourth Group: Miscellaneous								
Congenital heart disease, cardiac failure	7	3	4	78	+	....	3.00	....
Thyrotoxicosis, cardiac failure	20	2	5	34	+	....	1.50	....

Fiessinger [25] and Thiebaut [26] consider that this method is not sufficiently sensitive and are of the opinion that better results are obtained if the fractional elimination is studied during the twenty-four hours rather than the total figure of galactose. In addition to the partial concentration of each specimen, these authors take into account the total concentration, according to the following formula:

$$\frac{\text{total quantity of galactose in 24 hours} \times 1{,}000}{\text{volume of urine in 24 hours}}$$

Finally they express the results of the partial concentrations in grams per thousand and consider as normal a galactose elimination of not greater than 5 per cent in the first specimen and of 1 per cent in the second. In the third and fourth samples there should be no galactose at all.

This was the method followed by us, and the details of its technic are set down in the beginning of this paper.

The 17 completed cases, of which 15 showed decompensation and 2 did not, appear in table 8. It can be seen that 13 of the patients with heart failure had positive reactions and only 2 had normal reactions, 1 of them (27 bis) just as he showed improvement from his decompensation. A similar improvement reflected by the test was observed in 2 other patients who were cured of their heart failure, but these are not included in the table because study of these patients was not completed. Of the 2 compensated cardiac patients, 1 had a positive and the other a negative reaction.

25. Fiessinger, N.: Les explorations fonctionelles, Paris, Masson & Cie, 1935, p. 146.
26. Thiebaut, F.: Epreuves biologiques dans les ictères, Paris, Masson & Cie, 1932.

In 10 of the cases studied we compared Bauer's and Thiebaut's methods, and in only 1 case were the results concordant. The other 9, positive according to Thiebaut's method, had normal elimination rates according to Bauer's technic. We have pointed out too many sources of error in both methods as regards the decompensated cardiac patient for us to place full confidence in one rather than in the other of the two procedures.

GENERAL CONCLUSIONS

1. During heart failure the functions of the liver are profoundly disturbed. Blood bilirubin determinations and determinations of bromsulphalein and urobilinogen of the urine are positive as a rule, are perceptibly parallel to each other and usually keep a definite relationship with the degree of heart failure.

2. Tests which proved to be abnormal during heart failure turn back to normality when the latter disappears. When there is only an improvement of the circulatory condition, results follow an evolution which parallels such improvement.

3. In cases of heart failure, functional hepatic disturbance does not usually keep a definite relationship with the cause of the heart condition itself. However, according to employed tests, the most accentuated hepatic disturbances are usually found in the group with rheumatic heart disease.

4. The Takata-Ara test is deprived of specific value and is of no use to evaluate the functional capacity of the liver.

5. The test of induced galactosuria is too influenced by circulatory disturbances, which renders it valueless as a hepatic test in heart failure.

Paseo de la Reforma 211.

ABSTRACT OF DISCUSSION

DR. GEORGE HERRMANN, Galveston, Texas: This work reflects the ability of the clinicians of Mexico to recognize problems that we have neglected. Our free use of sugar and milk with its high calcium content and of xanthines in the presence of congestive failure might be a protection to the liver cells. Do our patients possibly have greater hepatic reserve? Somolinos-Artois stated recently in Mexico that the blood citric acid level was an index as to whether the functional disturbance of the liver was going to progress and the patient die or whether it was going to regress. His slides showed a tremendous destruction of the liver such as we rarely see in our cardiac patients. We would be prone to attribute such liver necrosis to some other cause. In the light of Professor Chávez and Dr. Sepúlveda's work we must more carefully study our patients with congested livers. Another point of interest was the preponderant number of patients with rheumatic heart disease in this series that showed liver disturbance. Rheumatic carditis, as Professor Chávez has described it, in Mexico is active much longer and is more severe than the rheumatic fever that we see in the Southwest. I should therefore like to know what percentage of these patients had tricuspid stenosis. An increased frequency of the tricuspid lesions might be one of the reasons why there is greater disturbance of the liver function in this series than we see in heart failure in the Southwest. The results of the galactose tests are surprising and indicate some disturbance in the important hepatic carbohydrate metabolism as well as the other functions. I don't believe that in Mexico they use sugar, milk and xanthines as freely in heart patients as we do. We have considered disturbances in the blood serum proteins as evidence of hepatic dysfunction and have found that a large number of our patients had lowered levels and disturbed plasma protein relationships. In some of these patients concentrated human blood plasma administered intravenously produced a diuresis and general improvement. Our cardiac patients suffer from protein undernutrition probably less than the Mexicans do, and I would venture to predict that a large number of them would show a decrease in the blood serum proteins in the presence of such severe hepatic disturbances along with congestive failure.

DR. A. P. MUNSCH, St. Louis: It was a pleasure to listen to this extensive report on the experimental work done by Dr. Chávez and his collaborators. I am not aware that such a report exists and more than one thing has happened as a result of it. It gives us a standard to go by in comparison and it calls attention to an important condition. I believe that nearly all cardiologists and medical men have remained in the background in considering the importance of liver function clinically in cardiac failure. We are all aware of the importance of the liver function. We are aware that in cardiac failure there is a pathologic congestion to a greater extent. We are also aware that any organ that is congested cannot function normally. Therefore the normal function of the liver is impaired. Dr. Chávez has shown us, through his commendable results from experimentation, a great deal about this damage. The realization of the points brought out by him will enable us to help at least to take the load off the damaged liver and in so doing lessen the embarrassment of the heart as well as that of the patient. He has given us an important thought and message to remember—that in cardiac failure it is important to consider the damaged liver function. It undoubtedly accounts for more deaths than we realize. As a result of his calling the attention of this audience to this subject, all of us will go away with a greater realization of its importance and with a happy memory of the doctor who came to us from Mexico City to wake us up on this matter.

DR. IGNACIO CHÁVEZ, Mexico City: Dr. Herrmann has reason when he says that there may be more hepatic reserve here among patients in the United States than in Mexico. Our pathologists are accustomed to seeing lesions in the liver at autopsy which are more severe than those seen in the hospitals of other parts of the world. It seems as if the livers of our people are much more damaged. I don't know whether it is due to deficiencies in the diet, alcohol or some other factor, but that is the fact. In heart failure we are accustomed to seeing the liver show not only greater congestion but greater destruction—necrosis and cirrhosis—than is normally seen in other countries. Dr. Herrmann also says that he is surprised at the great number of patients with rheumatic disease in comparison with the other forms of cardiopathy. That is true also. Among our poor, rheumatism is so widespread that it is the greatest cause of heart disease in Mexico. In Cleveland at the meeting of the American Heart Association I pointed out that in Mexico City, in the high altitude of our high plateau, is where the highest figure of rheumatic heart disease has ever been shown. In my own statistics of 2,400 organic cardiac cases, I have shown that 61 per cent of them in the charity hospitals are of rheumatic origin. It is 50 per cent more than in Boston, Washington, Paris or London. In no part of the world has there been shown so great an incidence of rheumatism in heart disease. As to the comments of Dr. Munsch, I can only say that we think that the liver in the cardiac patients passes through two periods. In the first period, when the heart failure begins, the liver trouble is reversible. It is only a functional attack. In the second period, when the lesion has been established, the tests are more and more abnormal while the heart condition is more advanced. The lesions are tremendous and they are of irreversible nature. That is the reason why sometimes, when the heart condition improves, the tests remain abnormal. A certain injury to the hepatic tissue remains. We do not employ any particular treatment for this liver condition while the heart failure is not ameliorated. We treat these patients as heart patients, and the only point that we have always in mind is not to give them digitalis by mouth when the liver is greatly congested. Our routine procedure is to give them digitalis by intramuscular or intravenous injection. When the heart failure disappears and the liver insufficiency persists, then it is necessary to use a certain treatment for this condition, depending on the grade and the type.

Clinical Notes, Suggestions and New Instruments

A HIGH PROTEIN BEVERAGE

LOUIS BAUMAN, M.D.
WITH THE TECHNICAL ASSISTANCE OF
MISS HERMALINE GAGE, B.S., NEW YORK

Low serum proteins are encountered in a number of conditions including diseases of the liver, kidney, stomach and intestine and during protracted convalescence from operations on the alimentary canal, e. g. after abdominal perineal resections of the rectum and in extensive and prolonged infections of burns. The ingestion of solid food by many of these patients is inadvisable or unacceptable, and the intravenous injection of proteins or amino acids over a prolonged period may not be entirely practicable or economical.

Therefore it seemed desirable to prepare a beverage that is rich in biologically important proteins. For this purpose we used a base of milk or evaporated milk to which egg white and powdered milk (Dryco) was added.

TABLE 1.—*Composition of the High Protein Mixture per Thousand Cubic Centimeters*

Ingredient	Grams	Carbohydrate, Gm.	Protein, Gm.	Fat, Gm.	Calcium, Gm.	Phosphorus, Gm.	Iron, Mg.	Vitamin A, International Units	Thiamine, Mg.	Vitamin C	Riboflavin, Mg.	Vitamin D, International Units
Milk	625	31	21	25	0.73	0.58	1.3	1,000	0.30	—	1.38	3-30
Dryco	150	69	48	18	1.50	1.22	...	3,150	0.54	—	—	495
Egg white	200	2	22	—	0.04	0.05	0.3	—	—	—	0.68	—
Total, 1,199 calories		102	101	43	2.27	1.85	1.6	4,150	0.84	—	2.06	500+
1 glass, 300 cc., 240 calories		20	20	9	0.45	0.37	0.3	830	0.17	—	0.41	100

Measures of food used: Milk..... 2½ cups
Egg whites (frozen)..... 1¾ cups
Dryco..... 1⅝ cups

TABLE 2.—*Recommended Daily Allowances for Specific Nutrients*

Food and Nutrition Board of the National Research Council

	Calories	Protein Gm.	Calcium Gm.	Iron, Mg.	Vitamin A, I. U.	Thiamine, Mg.	Riboflavin, Mg.	Nicotinic Acid, Mg.	Ascorbic Acid, Mg.
Man (70 Kg.), moderately active	3,000	70	0.8	12	5,000	1.8	2.7	18	75
Woman (56 Kg.), moderately active.....	2,500	60	0.8	12	5,000	1.5	2.2	15	70

The method of preparation is simple. It consists in mixing milk powder gradually with frozen egg white, which has been beaten until foamy (but not dry) with an egg beater and then adding the milk while the mixing process is continued. Filtration through one thickness of gauze will remove the egg membrane.

Such a mixture can easily be prepared in a field hospital from canned or dry material and can be fortified with vitamin concentrates or cream if added calories are required. The day's supply is prepared in the morning and kept cool in the refrigerator. When served, each glass may be sweetened with sugar and flavored with vanilla, chocolate, coffee, malt extract or molasses.

It is also a practical mixture in the medical treatment of duodenal ulcer. Most patients consume this mixture with relish, though occasionally a distaste for milk is encountered and considerable urging may be necessary.

In table 1 the composition of the mixture is given in detail. Table 2 shows the daily allowance for specific nutrients recommended by the Food and Nutrition Board of the National Research Council.

620 West 168th Street.

From the Departments of Surgery and Nutrition, Columbia University.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

WESTERN ELECTRIC ORTHO-TRONIC AUDIPHONE ACCEPTABLE

Manufacturer: Western Electric Company, 300 Central Avenue, Kearny, N. J.

The Western Electric Ortho-tronic Audiphone is a vacuum tube hearing aid with microphone and amplifier housed in molded plastic case. A and B batteries are contained in separate leather case. The weights and overall dimensions of various parts are as follows: 125 A-3 amplifier, 5¼ inches by 2¾ inches by ¾ inch, weight 5.75 ounces.

Battery case, 5¼ inches by 2½ inches by 1 inch, weight 12.8 ounces.

714–A, 714–B, 714–C } Air receiver, without molded earpiece, ⅞ inch by ⅜ inch diameter, weight 0.31 ounce.
715–A—Bone conduction receiver, 1⅜ inches by ¾ inch by 1 inch, weight 0.81 ounce.

Batteries: The current supply is: A battery, 1.5 volt, size D, drawing 90 milliamperes at full volume. B battery, 45 volt, No. 455, drawing 1.0 to 2.2 milliamperes under operating conditions.

Acoustical Gain: The microphone amplifier unit carries three controls, an on and off switch, volume control and "tone discriminator," operated by knurled disks at the top of the instrument. The volume control serves the usual purpose of regulating the degree of amplification, and the tone discriminator changes the degree of amplification as between the high and low frequencies. Curves submitted show that the shift from "full tone" to "minimum tone" position suppresses frequencies below 1,000 cycles much more than frequencies above this value. Tests verify this claim, as shown later. The following amplifications for intensity slightly above normal ear threshold give the order of magnitude of the increase of sound intensity levels at the ear of the wearer over that at the microphone under normal use.

Western Electric Ortho-tronic Audiphone.

They do not give the maximum possible gain under ideal conditions nor the electrical amplifications as shown by measurements of electrical input and output.

		Frequency				
Receiver	Tone Setting	128	256	512-2,048	3,000	4,096
714 A	Minimum	Nil	?	15-35	14	13 decibels
714 A	Maximum	Nil	26	30-48	17	13 decibels
714 B	Minimum	Nil	15	25-44	19	13 decibels
714 B	Maximum	Nil	19	36-46	23	13 decibels
714 C	Minimum	Nil	?	22-34	..	16.5 decibels
714 C	Maximum	Nil	13	29-42	..	15.0 decibels

Acoustical Feedback: The foregoing values were shown with volume setting approximately two thirds full on. As usually occurs in instruments showing high gain, the maximum gain attainable in use is determined by the closeness of the fit of the earpiece in the ear. Tests made, using a custom fitted earpiece, showed that a volume setting of five sixths of full volume was the maximum with receiver 714 A, tone control setting at maximum, and two-thirds full volume with tone control setting at minimum. With receiver 714 B, five sixths of full volume could be obtained without feedback for both maximum and minimum settings of tone control. Practically full volume could be obtained with 714 C receiver for both tone control settings.

Articulation: The usual syllable and sentence lists were used with a hard of hearing subject at a distance of 5 feet in a quiet room, with instrument set for comfortable hearing and using each of the three air conduction receivers and the bone receiver. These tests showed satisfactory performance for all combinations. The instrument is well made.

The Council voted to accept the Western Electric Ortho-tronic Audiphone for inclusion in its list of accepted devices.

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SATURDAY, APRIL 17, 1943

B_1 VITAMIN HYPOIMMUNITY

As part of a long range program of study of the relation of diet to virus infections, Foster and her co-workers [1] of the University of Pennsylvania studied the relative susceptibility to poliomyelitis of mice maintained at different levels of vitamin B_1 (thiamine) intake. At the luxury level mice were given diets containing 100 micrograms of thiamine per hundred grams of food, which more than covered their full nutritional requirements (thiamine excretion not determined). Other groups of mice were maintained on a diet containing as little as 10 micrograms of thiamine per hundred grams. This usually led to signs of deficiency within fifteen days, with death of 40 per cent of the mice within thirty days. Still other groups were given thiamine at the minimum maintenance level, after partial depletion at the 10 microgram level, their thiamine intake being increased to 30 micrograms per hundred grams. The majority of these animals remained healthy and at stationary body weight for at least thirty days. After from fifteen to thirty-four days on these differential diets each animal was inoculated intracerebrally with 0.03 cc. of a 0.5 per cent suspension of poliomyelitis infected mouse brain, control inoculation being made with uninfected brains.

In a typical experiment 36 mice were maintained for thirty-four days at the luxury thiamine level. On inoculation with the routine test dose 30 mice (83 per cent) developed typical paralysis, from which all died within thirty days, 3 additional mice (8 per cent) of the group dying without showing paralytic symptoms. A parallel group of 24 mice were maintained at the deficiency (10 microgram) thiamine level. On inoculation but 4 mice of this group (16 per cent) developed lethal paralysis, while 6 mice (25 per cent) died without showing paralytic symptoms, control tests suggesting that these additional deaths were due to thiamine deficiency.

In this experiment the incidence of lethal paralysis was increased fivefold as a result of the luxury vitamin B_1 intake (or decreased fivefold as a result of thiamine deficiency). Even more striking results were obtained in a second experiment, in which comparison was made with mice maintained at the 30 microgram level. Here there was a sevenfold increase in the number of lethal paralyses at the luxury vitamin B_1 level, when compared with the number at the minimum (30 microgram) maintenance level. If one should take the average of all groups, their data suggest a sixfold increase in poliomyelitis susceptibility as a result of a slight excess of vitamin B_1 (or a sixfold increase in resistance as a result of vitamin B_1 subnutrition). Thus viewed, urinary excretion of excess thiamine [2] becomes a purposeful defensive mechanism to prevent thiaminogenic viral hypoimmunity.

Thus far the Pennsylvania pediatricians have avoided offering a theoretical explanation of this wholly unexpected phenomenon. In their opinion the length of survival of the virus and the nature of the histologic lesion in thiamine deficient mice must be determined before a definite theory can be formulated. It would be in line with the present tendency in immunologic research, however, to assume that thiamine is a necessary nutritional factor for the symbiotic multiplication of the polio virus, a relative abundance of thiamine leading to its increased proliferation, with thiamine subnutrition inhibiting proliferation. Such a theory would be essentially a renaissance of the original Pasteur exhaustion theory of acquired immunity, a discarded theory now being reconsidered by numerous investigators, particularly in its application to the phenomenon of virus antagonism.[3]

For some time a somewhat similar phenomenon has been under investigation by plant pathologists. Growers of narcissus bulbs, for example, have attempted to obtain superior flowers, increased bulb production and increased disease resistance by the use of numerous artificial plant hormones or synthetic growth stimulants. Stuart and McClellan [4] of the U. S. Department of Agriculture tested such possibilities. To their disappointment they found that, far from protecting bulbs from disease, such growth hormones stimulated the growth and apparently increased the pathogenicity of basal rot fungus (Fusarium oxysporum f. narcissi) and thus increased commercial loss from basal rot.

That thiamine has a somewhat similar stimulating effect on the poliomyelitis virus is the essential tentative suggestion from the results that have been reported by the Pennsylvania pediatricians. Whether or not vita-

1. Foster, Claire; Jones, J. H.; Henle, Werner, and Dorfman, F.: Proc. Soc. Exper. Biol. & Med. **51**: 215 (Nov.) 1942.

2. Thiamine Requirement of Man, editorial, J. A. M. A. **121**: 53 (Jan. 2) 1943.

3. Poliomyelitis Inhibition, editorial, J. A. M. A. **121**: 194 (Jan. 16) 1943.

4. Stuart, N. W., and McClellan, W. D.: Severity of Narcissus Basal Rot Increased by the use of Synthetic Hormones and Nitrogen Bases, Science **97**: 15 (Jan. 1) 1943.

min B_1 possesses a similar synergistic action with other viruses, when it is tested in other animal species or by other methods of injection, however, has not yet been determined.

The difference between the sevenfold and fivefold ratios drawn from Foster's data suggests the tentative conclusion that the maximum natural resistance to poliomyelitis virus is obtained from a minimum full maintenance level of vitamin B_1 intake and that intakes either above or below this level cause decreased resistance. If this should be confirmed by future tests, it would form a new rational basis for dietary hygiene and clinical therapy.

SUNLIGHT CARCINOMA AND OTHER TUMORS INDUCED BY ULTRAVIOLET RADIATION

Tumors of the skin of exposed parts of the human body in most cases are epidermal carcinoma, mostly of the squamous variety. Clinical observations and statistical study support the view that the most important cause of this carcinoma is sunlight, specifically the ultraviolet rays of the spectrum. For instance, more carcinoma of the exposed skin of white men occurs in the southern than in the other parts of this country. Farmers, sailors and other outdoor workers are more frequently victims of such carcinoma than persons less exposed to sunlight. Experiments have shown, moreover, that cancer of the skin as well as of other tissues is easily induced in albino mice and other animals by ultraviolet radiation under well controlled conditions. It has been found by Blum and his co-workers [1] at the National Cancer Institute that in mice ultraviolet radiation penetrates the skin to some depth and thus can act on a variety of cells, inducing different kinds of tumors.

The most recent analysis of the results of extensive experiments by Blum and his associates [2] showed that spindle cell sarcoma predominated while squamous carcinoma formed a smaller group often combined with sarcoma. Also hemangioendothelioma, osteochondrosarcoma, sebaceous carcinoma and even tumors of the eye developed in mice exposed to ultraviolet radiation, indicating that ultraviolet rays can induce tumors in various tissues depending on their susceptibility to its action and limited by the penetration of the rays. It would seem, then, that ultraviolet radiation can induce tumors in any susceptible tissue it may reach.

Why do not other forms of tumor besides epidermal carcinoma develop frequently in men freely exposed to sunlight? The reason appears to be that in man the amount of radiation reaching the dermis at best is not sufficient to induce the growth of tumors—sarcoma, and so on—of cellular elements in the dermal tissue. The workers at the National Cancer Institute found that the transmission of carcinogenic wavelengths by the human epidermis is much lower than by the mouse epidermis. In fact, in well tanned human skin almost no rays could reach the dermis. That white persons, especially blonds, seem more susceptible than Negroes to carcinoma of the exposed skin suggests that the pigment in the epidermis protects against the carcinogenic effect of ultraviolet rays.

1. Blum, H. F., and Lippincott, S. W.: Carcinogenic Effectiveness of Ultraviolet Radiation of Wavelength 2,537A, J. Nat. Cancer Inst. **3**: 211 (Oct.) 1942. Kirby-Smith, J. S.; Blum, H. F., and Grady, H. G.: Penetration of Ultraviolet Radiation into Skin as a Factor in Carcinogenesis, ibid. **2**: 403 (April) 1942.
2. Grady, H. G.; Blum, H. F., and Kirby-Smith, J. S.: Types of Tumor Induced by Ultraviolet Radiation and Factors Influencing Their Relative Incidence, J. Nat. Cancer Inst. **3**: 371, 1943.

VITAMIN E DEFICIENCY

Evans and Bishop [1] in 1923 concluded that certain natural foods, notably wheat germ and many plant leaves, contain a factor essential for normal reproduction in the rat. This substance, later called vitamin E, was shown to be essential for the successful completion of intrauterine growth as well as for the maintenance of testicular function in the male. The female mouse, like the rat, shows typical resorption of the fetuses when restricted to vitamin E deficient rations, whereas in the male mouse degenerative changes in the germinal tissues of the testes have not been demonstrated.[2] Again eggs from hens on a diet poor in vitamin E show early embryonic mortality and low hatchability. Vitamin E has been isolated, characterized chemically and synthesized; while the name alpha tocopherol has been given to an alcohol obtained from wheat germ oil, several other compounds possess similar biologic activity. Other functions have been demonstrated for the tocopherols during the past decade, but the part they play in promoting successful reproduction seems to have characterized these compounds from the functional point of view.

The striking gross feature of the reproductive failure in the female white rat restricted to diet deficient in vitamin E is the death and resorption of the fetuses when about two thirds of the gestation time has elapsed. In subsequent matings the same phenomena are seen unless vitamin E is administered, when normal reproduction again ensues. Adamstone [3] observed that in eggs from hens on feed poor in vitamin E the chick fails to hatch because of the development of a so-called lethal ring in the blastoderm, formed from cell proliferation in the mesoderm. This obstructs the blood vessels of the blastoderm and they disintegrate; the embryo dies from hemorrhage, ischemia and starvation. The mechanism of embryonic death in the mammal on diets deficient in tocopherol has recently been elucidated by Mason.[4] In a large number of observations on 16 day old rat embryos he observed widespread hemorrhages on the surface in the head, shoulder and trunk

1. Evans, H. M., and Bishop, K. S.: Am. J. Physiol. **63**: 396, 1923.
2. Bryan, W. L., and Mason, K. E.: Am. J. Physiol **131**: 263 (Nov.) 1940.
3. Adamstone, F. B.: J. Morphol. & Physiol. **52**: 47 (Sept. 5) 1931.
4. Mason, K. E.: J. Nutrition **23**: 59 (Jan.) 1942; Yale J. Biol. & Med. **14**: 605 (July) 1942.

regions in plexiform patterns. The lesions were characterized by vasodilatation, congestion and vascular stasis of the superficial blood channels with subsequent bleeding into the various parts of the central nervous system. The general conclusion is reached that there develops in this specific nutritional deficiency a structural weakness of the vascular system leading to stasis and that death is due to the consequent progressive ischemia of the fetal tissues.

Elucidation of the biochemical defect induced by a deficiency in vitamin E is significant not only on its own account but also because it helps to temper the conception of functional specificity of the vitamins. Particularly important is recognition of the extent to which the tissues of the body are sensitive to slight chemical changes in the blood and lymph on which their metabolism depends.

Current Comment

RENAL VASCULAR DISEASE AND HYPERTENSION

The demonstration by Goldblatt [1] that chronic hypertension regularly follows partial clamping of the renal arteries of dogs and by Moritz and Oldt [2] that people with chronic hypertension usually show diffuse renal arteriolar sclerosis at necropsy, whereas normal persons rarely have such sclerosis, suggests that renal vascular disease in man may be the etiologic counterpart of the Goldblatt clamps in the dog. Although it has been recognized that degenerative vascular disease often follows the appearance of hypertension, the new evidence lends support to the view that renal vascular disease may often be primary and causal. A recent study of renal biopsies from 100 human subjects incident to the performance of splanchnic resections for hypertension afforded Castleman and Smithwick a unique opportunity to investigate an earlier stage of the disease than had been theretofore studied. Although all their patients had severe chronic hypertension, the renal vascular disease observed in 53 was so slight that it seemed unlikely in the opinion of the authors "that the blood flow could have been embarrassed sufficiently to be the one factor responsible for the hypertension." Thus it would appear that most if not all of the degenerative arteriolar lesions observed in persons dead of the effects of chronic hypertension should probably be regarded as secondary rather than primary. The observations of Castleman and Smithwick [3] provide some degree of morphologic confirmation of the conclusions of Homer Smith [4] and his associates, who found from renal blood flow studies that "there exists a perturbation of vascular function which is primary in time and causality to the destruction of renal parenchyma." Whether the renal arteriolar lesions represent the late structural manifestation of a primary "perturbation of vascular function" or the mechanical effects of a prolonged elevation of intravascular pressure is not yet clear.

1. Goldblatt, Harry: Experimental Hypertension Induced by Renal Ischemia, Harvey Lectures, Baltimore, Williams & Wilkins **33**: 1937-1938.
2. Moritz, A. R., and Oldt, M. R.: Arteriolar Sclerosis in Hypertensive and Nonhypertensive Individuals, Am. J. Path. **13**: 679 (Sept.) 1937.
3. Castleman, Benjamin, and Smithwick, R. H.: The Relation of Vascular Disease to the Hypertensive State Based on a Study of Renal Biopsies from 100 Hypertensive Patients, this issue, p. 1,256.
4. Smith, H. W.: Physiology of the Kidneys, Dept. of Journalism Press, University of Kansas, Lawrence, 1939.

BOTULISM

Meyer and his associates in California have gathered statistics on 367 outbreaks of botulism in the United States since 1899. Only 83 of the outbreaks have been due to commercially canned foodstuffs; with one possible exception, outbreaks have not occurred in nearly twenty years from this source. The other 284 outbreaks have been caused by foods canned in the home. The total cases of the disease for the forty-three years numbered 1,052 with 687 deaths, a fatality rate of 65 per cent. How many other unrecognized cases have occurred is unknown. During the coming canning season many persons who never before attempted home canning will preserve garden produce. The danger from botulism is ever present unless proper precautions are taken. Faust,[1] discussing methods of home canning, emphasizes the necessity of the pressure cooker with an accurate gage or thermometer for nonacid foods, such as string beans and corn. Any such foods that have been processed in any other manner must be reboiled for at least fifteen minutes before tasting or using. Any home canned food that shows the slightest evidence of spoilage should not even be tasted, for the toxin of the botulinus bacillus is the most powerful poison known. The problem calls for concerted effort by agricultural advisers and public health personnel in warning against faulty methods of home canning and alertness of physicians in recognizing symptoms and administering antitoxin early and in adequate amounts.

1. Faust, Hilda: Nutrition Program During the War—Home Canning, University of California College of Agriculture, Berkeley.

MARMOLA IS DANGEROUS TO HEALTH

Any drug which may expose the users to disease and pain when taken in the dosage and with the frequency recommended and suggested in its labeling is dangerous to health. Marmola is such a drug, held the U. S. District Court for the Western District of Wisconsin in a recent case.[1] This proceeding was predicated on the contention that the article was dangerous to health when used in the dosage or with the frequency prescribed, recommended or suggested in its labeling and on the further ground that the labeling was false and misleading because it failed to reveal facts material with respect to the consequences which might result from the use of the article under the conditions of use prescribed therein. In sustaining the goverment's contentions, the court pointed out that a substantial portion of the public, after reading the labeling used in connection with the product, would conclude that obesity is caused by the lack of some substance in the human body that Marmola supplies and that Marmola is a safe and efficient remedy for obesity, which is not a fact.

1. U. S. v. 62 Packages, More or Less, of Marmola Prescription Tablets, decided Feb. 23, 1943 by the District Court of the United States for the Western District of Wisconsin (No. 139 Admiralty).

The administration of thyroid in the dosage contained in Marmola, the court thought, constitutes a dangerous procedure which should not be undertaken without a thorough examination of the prospective user by a competent physician and then only under the supervision of the physician. While the federal act was not intended to prevent self medication, the court observed, it was enacted to make self medication safer and more effective. An imposing list of expert witnesses testified in this case for the government and for the intervener, the Raladam Company. The decision of the court lists these witnesses without in most instances indicating the exact nature of the testimony they offered. Among those testifying for the Raladam Company were:

Dr. Abbott W. Allen, New York, assistant clinical professor of medicine of Columbia University; Dr. John A. Killian, Englewood, N. J., professor of biochemistry at the New York Post-Graduate School of Columbia University; Dr. Plinn T. Morse, Detroit, consulting pathologist; Dr. William A. Spitzley, general practitioner; Dr. Benjamin H. Schlomovitz, Milwaukee, professor of pharmacology and toxicology, Marquette University Medical School, and Dr. Andrew I. Rosenberger, Milwaukee, a specialist in diseases of the nervous system.

Among the witnesses who offered testimony in support of the government's contentions that the distribution of Marmola in interstate commerce was unlawful were:

Dr. James Short, New York, and Dr. Frank Stites, Louisville, Ky., both specialists in internal medicine; Dr. Elmer L. Sevringhaus, Madison, Wis., professor in the Medical School of the University of Wisconsin and a specialist in metabolic and endocrine diseases; Dr. Willard O. Thompson, Chicago, professor in the Medical School of the University of Chicago and a specialist in endocrinology and metabolism; Dr. Louis H. Newburgh, Ann Arbor, Mich., professor in the Medical School of Michigan University and a specialist in endocrinology and metabolic diseases; Dr. Israel Bran, Philadelphia, a specialist in thyroid diseases; Dr. Russell M. Wilder, Mayo Clinic, an instructor in the Medical School of the University of Minnesota and a specialist in the treatment of diabetes; Dr. Samuel F. Haines, Mayo Clinic, head of the section of the clinic pertaining to thyroid diseases and associate professor at the University of Minnesota; Dr. William Oatway, Madison, Wis., a member of the faculty of the Medical School of the University of Wisconsin; Dr. Chester M. Kurtz, Milwaukee, a member of the faculty of the Medical School of the University of Wisconsin and a specialist in heart diseases; Dr. Anton J. Carlson, Chicago, who formerly held a professorship in the Department of Physiology at Rush Medical College and the University of Chicago from 1904 until recently, when he retired, and Dr. Marian S. Kimble, Madison, Wis., a chemist who, as an investigator, made tests as to the value of desiccated thyroid as a remedy for obesity.

One of the concluding paragraphs in the court's opinion merits a direct quotation:

The Court is thoroughly convinced, by a preponderance of the evidence, that Marmola, when used as prescribed in the labeling thereof, is neither a safe, appropriate nor an efficient remedy for obesity; that it is dangerous to the health of the user when used in the dosage or with the frequency and duration prescribed, recommended or suggested in the labeling thereof; that the packages of Marmola in question, when seized in these proceedings, were misbranded within the meaning of the sections of the Federal Food, Drug and Cosmetic Act involved herein; that the labeling on Marmola is false and misleading in its representations that it is a safe remedy for obesity, and in that it fails to reveal facts material with respect to consequences which may result from the use of Marmola under the conditions prescribed in the labeling.

Thus unfolds another chapter in the existence of a preparation the dangers of which have been repeatedly pointed out in THE JOURNAL and which has received the attention of the federal government for over a decade. If this is not the final chapter, how long will it go on?

SWINE LUNGWORM AS RESERVOIR FOR SWINE INFLUENZA VIRUS

Shope's work on the swine lungworm as a reservoir and intermediate host for the virus of swine influenza adds a significant observation to research on viruses. In his most recent paper he [1] reports ninety-eight experiments with transmission, using 216 swine and involving a three year study of the lungworm as an intermediate host for the virus of swine influenza. Fifty of the experiments gave negative results. In the remaining forty-eight transmission of virus by way of the lungworm was demonstrated in 1 or more animals of each experiment. Irregularities in the results, Shope explains, would appear to be due not so much to lack of transmission of the masked virus by the lungworms as to failure to evoke its pathogenic capabilities. In several experiments pigs developed infections with the virus of swine influenza nine to seventeen days after infestation with infected lungworms, in the absence of any known provocative stress. An immune response of the swine to the lungworms themselves is suspected in these instances of having furnished the provocation. During the summer months May to August inclusive swine prepared by the injection of lungworms carrying virus were absolutely refractory to the provocation of influenza. They were also relatively refractory in September and October. Activation of the masked virus occurred most readily during the first four months of the year. In one experiment it was possible to demonstrate by direct means the presence of virus in the neighborhood of lungworms at the base of the lung at a time when the virus could not be demonstrated anywhere else in the respiratory tract. Masked virus of swine influenza was found to be present in lungworm ova obtained either from the respiratory tracts or from the feces of infected swine. In several instances masked virus persisted for over a year in lungworm larvae within the earthworm intermediate host, and in one of these its presence was demonstrated after thirty-two months. Finally it was found that lungworm ova obtained from convalescent swine which no longer carry swine influenza virus in infectious form in their respiratory tracts contain a masked virus. Such observations as these on the behavior of swine influenza virus are of doubtful immediate significance in relation to human influenza, though they clearly extend knowledge of the behavior of viruses. Furthermore swine influenza itself, although not a highly fatal disease, has some intrinsic importance to the national economy and the veterinary profession.

1. Shope, Richard E.: The Swine Lungworm as a Reservoir and Intermediate Host for Swine Influenza Virus, J. Exper. Med. 77: 111 (Feb.) 1943.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

RESTRICTIONS ON USE OF INTERNS AND RESIDENTS

Because the number of interns and residents available for the year 1943-1944 will be very limited, the hospitals of the United States will have to reduce the number of such personnel to approximately 50 per cent of the number they maintained in 1940, it is announced by the Directing Board of Procurement and Assignment Service, acting on the advice of its Committees on Hospitals and the Allocation of Medical Personnel.

The following recommendations have been issued by the Directing Board of the Procurement and Assignment Service to its state chairmen:

For the efficient utilization of attending physicians, interns and residents, hospitals should avoid duplication of activities such as two or more medical, surgical or other surgical services, by consolidating such parallel services into one.

Hospitals should be requested also to arrange for the reabsorption of clinics in the subspecialties into a general clinic of the parent specialty and to maintain within the structure of the medical staff, in both inpatient and outpatient services, only such specialties as are recognized by the Advisory Board for Medical Specialties.

A hospital should not have more interns on July 15, 1943 than the number on duty on July 15, 1940 unless it can be shown that the institution's patient load has definitely increased or that other conditions exist that merit special consideration. Hospitals which have had a decrease in their patient load since July 15, 1940 should make a corresponding decrease in the number of interns.

In order to provide an adequate background for military medical service, at the completion of one year of internship, hospitals which do not now maintain rotating internships should, for the duration of the war, broaden and diversify the instruction and experience of their interns.

A physician who is eligible for military service should not be approved as an essential resident in a hospital unless the residency concerned is approved by the appropriate crediting body.

A physician who is eligible for military service should not be approved as an essential resident in a hospital for longer than a period of one year immediately following the completion of his internship. Physicians who by age, sex, physical defect or citizenship status are disqualified for military service may serve as residents in hospitals for periods varying from one to three years after internship. After this period of service such physicians, if they are to be approved by the Procurement and Assignment Service as essential, must have been appointed as full time members of the regular medical staff.

After July 1, 1943 the total number of residents permitted for the hospitals of the United States shall not exceed 50 per cent of the number on duty in the hospitals on July 15, 1940; this 50 per cent shall include those residents who are not eligible for military service, e. g. women physicians, physically disqualified male physicians, older physicians and alien physicians.

In view of the considerable number of physicians not qualified for military service who should be available for appointment as hospital residents, all hospitals should fill as nearly 100 per cent as possible of their allotted residencies with physicians not eligible for military service.

The total number of residents which a hospital may be permitted to retain shall be directly related to that hospital's teaching and service responsibilities, with particular reference to the proportion of its ward service to total service. Consideration of an individual resident should be based primarily on his teaching responsibilities and patient service load and not on any specialized service which he may render to individual members of the staff or to a particular hospital service. A hospital shall not be permitted to retain a greater percentage of the number of its residents which it had on July 15, 1940 than the percentage of its ward patient days in relation to its total patient days; except that a hospital shall not retain more than two-thirds the number of the residents it had on July 15, 1940.

Ward service is defined as service to patients who are not charged or paying a professional fee and patients who are used for teaching demonstration, if a teaching program is being conducted. In computing the service load, the volume of outpatient visits shall be given due consideration.

Primarily teaching hospitals, i. e. hospitals carrying major responsibility for undergraduate medical teaching, shall be given consideration for that service in addition to that which they receive on the basis of ward service. A hospital which has made radical changes in bed capacity or in its intern and residency plans or has lost an excessive proportion of its visiting staff since July 15, 1940 may receive special consideration in the number of residents it is permitted to retain.

The Central Office of the Procurement and Assignment Service shall determine the total number of residents to be allotted to each state and shall suggest for the guidance of the respective state chairmen the number of residents recommended for each hospital after July 1, 1943.

Hospitals which find it necessary to request permission to retain, for a residency, an intern who holds a commission in military service shall submit such request to the state chairman for physicians of the Procurement and Assignment Service, who will add his recommendations and forward it to the Central Office of Procurement and Assignment Service for action by the directing board and for recommendation by the Army and Navy.

As far as possible, physicians who hold reserve military commissions for whom requests for further deferment have been made shall be assigned to residencies which will provide training of greatest usefulness in their subsequent military service, e. g. in surgery or medicine rather than in obstetrics and gynecology.

In order to accomplish these objectives, all residents must be selected from the following groups:

1. Women physicians.

2. Male physicians who have been officially rejected for commissioned service with the Army or Navy.

3. Male physicians who have been classified 4-F by Selective Service.

4. Physicians who have applied for commission in the Medical Corps of the Army of the United States or the Naval Reserve and whose deferments are being requested for the ensuing year, as outlined.

Hospitals should be instructed not to communicate with the Army or the Navy regarding deferment of reserve officers for further hospital service. Such communications should always be addressed to the state chairmen of the Procurement and Assignment Service.

PROCUREMENT OF SANITARY ENGINEERS

Paul V. McNutt, chairman of the War Manpower Commission, has issued a directive placing the procurement and assignment of sanitary engineers for the armed forces and other governmental agencies under the War Manpower Commission's Procurement and Assignment Service for Physicians, Dentists and Veterinarians.

Plans are already under way to facilitate the recruitment of sanitary engineers by the armed forces without endangering public health by clearing all sanitary engineers through the Procurement and Assignment Service, as is done with physicians, dentists and veterinarians.

A critical shortage of trained sanitary engineers exists as a result of the need of the armed forces for the services of these engineers who are trained in disease prevention and health protection, particularly in those parts of the world where the armed forces are encountering disease hazards resulting from improper sanitation and in many instances from insects peculiar to a particular region.

To meet these needs of the armed forces, many of the state, county and local health organizations, as well as concerns employing sanitary engineers, have been heavily drawn on. To make the best use of the dwindling number of sanitary engineers for military, semimilitary and civilian purposes, it has been found necessary to establish a more uniform system of procurement and assignment of such professional personnel than has been applied up to this time. Accordingly, the War Manpower Commission has set up in the Procurement and Assignment Service for Physicians, Dentists and Veterinarians a Committee for Sanitary Engineers to be made up of the following members:

Abel Wolman, chairman, professor of sanitary engineering, the Johns Hopkins University, Baltimore.
Kenneth F. Maxcy, professor of epidemiology, School of Hygiene and Public Health, the Johns Hopkins University, Baltimore.
Harold E. Babbitt, professor of sanitary engineering, University of Illinois, Urbana, Ill.
F. C. Bishop, assistant chief, Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture, Washington, D. C.
V. M. Ehlers, chief engineer, Texas State Board of Health, Austin, Texas.
Gordon M. Fair, professor of sanitary engineering, Harvard University, Cambridge, Mass.
H. A. Whittaker, chief engineer, Division of Sanitation, State Department of Health, Minneapolis.

Mr. Paul Hansen, consulting engineer of Chicago, has been appointed as civilian consultant. C. W. Klassen of the Army Sanitary Corps and formerly chief sanitary engineer of the Illinois State Department of Health, is being assigned by the Army to the War Manpower Commission to handle sanitary engineering procurement under Dr. Max Lapham, executive officer of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians.

For the purpose of administering this directive by the War Manpower Commission, the professional occupation designation "sanitary engineer" shall apply to a graduate of an approved scientific school who has fitted himself by suitable training or study and by experience to conceive, design, operate, direct or manage engineering works (*a*) developed as a whole or in part for the protection and promotion of the public health or (*b*) capable of injuring the public health through faulty conception, design, construction, operation or management. The basis for differentiation between individuals qualified as sanitary engineers and those qualified only as civil, mechanical, electrical, mining or chemical engineers shall be the ability to identify, evaluate and explain in terms of their sanitary or public health implications those factors connected with such engineering works as will prevent injury to health or will promote health in addition to the ability to conceive, design, operate, direct or manage such works.

All sanitary engineers coming within the scope of this occupational definition are urged to place their names on file with the War Manpower Commission and for this purpose and for any further information should communicate with the Procurement and Assignment Service, War Manpower Commission, 1006 U Street N.W., Washington, D. C.

The functions of the Procurement and Assignment Service in regard to sanitary engineers will be:

1. To determine the military and civilian needs for sanitary engineering personnel for this country and abroad.

2. To estimate the availability of sanitary engineering personnel of various ages and grades of experience.

3. To establish a plan for a well balanced allocation as far as practicable to meet the civilian and military needs.

PHYSICIANS' PREFERENCE IN CHOICE OF MILITARY SERVICE

A recent memorandum from the Officer Procurement Service of the War Department states that physicians, dentists and veterinarians are afforded an opportunity on the reply cards sent to them by the Central Office of the Procurement and Assignment Service to indicate a preference for service with the Army, including the Medical Department of the Army Air Forces, or the Navy. Preference so expressed by a candidate for service with the Medical Department of the Army Air Forces will be plainly indicated on form 97 by the state Procurement and Assignment chairman when that form is transmitted to a district office.

Effective immediately, each district office, in forwarding to the Surgeon General the completed papers of any candidate who has expressed a preference for Army Air Forces service, will include therewith a clear statement that the candidate has expressed a preference for service with the Medical Department, Army Air Forces.

District offices will not attempt to influence a candidate one way or the other. If there is no information in regard to preference on a candidate's form 97, the interviewing officer will not request information as to his preference. If a candidate requests information relative to assignments, the interviewing officer will inform him of his right to state, if he so desires, a preference. The district office is responsible for recording and forwarding the facts as to a candidate's preference, if any, in accordance with the foregoing.

In discussing assignments with candidates, interviewing officers will at all times make it clear that, while every consideration will be given to a candidate's expressed preference, there can be no assurance that he will receive the assignment requested. Assignments are based on the candidate's qualifications and existing needs.

THE QUOTA FOR DENTISTS

A wartime ratio of 1 dentist to each 2,500 civilian population has been established by the War Manpower Commission's Procurement and Assignment Service for Physicians, Dentists and Veterinarians in establishing state quotas for the 6,689 practicing dentists that will be required to meet the needs of the armed forces in 1943, the *Journal of the American Dental Association* reports. The total needs of the armed forces for the current year will be 9,500 dentists. The Procurement and Assignment Service points out that 3,616 of these will be obtained from 1942 and 1943 dental graduates, leaving 5,884 practicing dentists who will have to be obtained from the various states. In addition, 805 dentists still are to be inducted as of Nov. 30, 1942 to fill the quota for last year.

The Committee on Dentistry of the Procurement and Assignment Service reports that 1942 and 1943 dental school graduates who are commissioned in the armed forces are not to be credited against the quotas of the states in which they reside but against a central quota. The 5,884 dentists to be obtained among practicing dentists have been distributed in proportion to the dentists in each state. As of Nov. 30, 1942 thirty-two states had exceeded their first quotas by 1,283; however, Alabama, Arizona, Arkansas, Delaware, Florida, Georgia, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, Texas and Virginia had contributed dentists in excess of the sum of their 1942 and 1943 quotas.

ARMY

THE BORDEN GENERAL HOSPITAL

The new U. S. Army Borden General Hospital at Chickasha, Okla., of 1,003 beds was completed on January 15. The buildings are of wood cantonment type construction with outside asbestos sheathing. The total number of buildings is 135, which includes the theater of operation type buildings and barracks for the numbered field hospital that will be attached. The hospital has been named in honor of the late Lieut. Col. William Cline Borden, distinguished officer of the Medical Corps.

The medical officers on duty at the hospital are as follows:

COLONELS

Ernest R. Gentry, Commanding Officer
William H. Gordon, Chief, Medical Service

MAJORS

Clarence E. Bird, Chief, Surgical Service
Edmond L. Faust, Assistant Chief, Surgical Service
John B. Hunter, Surgical Service Assistant
Felix Jansey, Chief, Orthopedic Section
Kerwin M. Marcks, Chief, Plastic Surgery Section
Leslie E. Morrissett, Chief, E. E. N. T. Service
Nathan Muskin, Chief, Section General Medicine no. 1
Leo V. Schneider, Chief, Section, General Medicine no. 2
Silas H. Starr, Chief, Officers' and Women's Section
Aloysius T. Waskowicz, Post Executive Officer

CAPTAINS

James B. Berardi, Chief, Section on Cardiovascular Renal Diseases
Richard C. Cooke, Chief, Neurology and Psychiatry Section
Karl D. Dietrich, Chief, Septic Surgery Section
Leonard Freeman, Ward Surgeon
Sidney Gelman, General Medicine no. 2, Allergy, Acute Exanthematous Diseases
Samuel C. Gillespie, Officers' and Women's Section
Kenneth G. Jahraus, Chief, Anesthesia Section
James E. Kahler, Chief, Laboratory Service
Frank Kaminsky, General Medicine no. 1
Miles F. Kelly, Mess Officer
Daniel M. Kingsley, Ward Officer, Orthopedic Section
Wilfrid J. Lewis, General Medicine no. 2, Dermatology, Syphilology, Acute Upper Respiratory Disease
Hirsch R. Liebowitz, Chief, Gastroenterology Section
William J. MacFarland, Chief, X-Ray Service
Francis L. McPhail, Ward Officer, Orthopedic Section
Arthur H. Milbert, Chief, Urologic Section
Dolbert A. Minder, Ward Officer, Surgical Service
Ira S. Pidgeon, Ward Officer, Urologic Section
Gleen S. Rost, Ward Officer, Surgical Service
John W. Shadle, General Medicine no. 1, N. P. Section
Sanders K. Stroud, E. E. N. T. Assistant
Lee D. Van Antwerp, Registrar
George K. Wever, Cardiovascular Renal Diseases
Harry T. Zankel, Chief, Physical Therapy

FIRST LIEUTENANTS

Eugene W. Black, Anesthesia Section
Howard C. High Jr., E. E. N. T. Service
Oscar B. Hunter Jr., Assistant Chief, Laboratory Service
Max E. Johnson, Neurology, Neuropsychiatric Section
William P. Parrilli, Neuropsychiatric Section
Allan E. Walker, Gastroenterology Section

The chief nurse is Capt. Helen V. Johnson of the Army Nurse Corps.

The medical officers on duty with the 49th General Field Hospital, attached, are:

COLONEL

John L. Kantor, Commanding Officer

MAJOR

Isaiah A. Wiles, Executive Officer

CAPTAINS

Samuel S. Caplin
Frederick R. Mallott, Adjutant
Milton H. Omstead, Assistant Executive Officer

OFFICERS FROM THE RANKS

Companies C and D of the Medical Administrative Corps Officer Candidate School at the Medical Replacement Training Center, Camp Barkeley, Texas, graduated on March 24. Participating in the ceremony were Brig. Gen. Roy C. Heflebower, commandant; Col. George E. Armstrong, assistant commandant; Lieut. Col. Charles L. Driscoll, executive officer, and the band and color guard. Men selected from the ranks to attend officer candidate school are chosen for their qualities of leadership, initiative and intelligence, regardless of their educational background. On completion of an intensive twelve weeks training course these M. A. C. officers take over nonmedical functions formerly performed by medical and dental officers, thus releasing them for professional duties with field troops. On completion of a ten day leave, the newly commissioned second lieutenants will report to their first station assignments.

GENERAL DAVIS VISITS HOSPITALS

Brig. Gen. Addison D. Davis, commandant of the Medical Field Service School, Carlisle Barracks, Pennsylvania, and Col. Albert S. Dabney, assistant commandant, returned on April 1 from a trip through the South and Midwest, where they visited medical installations to observe the results of the courses of training for officers at the Medical Field Service School. At each station visited these officers sought out the Carlisle trained officers, whose training the commanding officers of the various posts praised highly. At the Medical Replacement Training Center at Camp Robinson, Arkansas, they observed 101 graduates of the Officer Candidate School at Carlisle Barracks. Brig. Gen. James E. Baylis, commandant of the training center, said that these medical administrative corps officers exhibited training of a high order. General Davis and Colonel Dabney visited also six general hospitals, several station hospitals, a school for aviation medicine, a port of embarkation and a great medical supply depot. They observed that in many cases the station hospitals were larger than the general hospitals. The aim of the medical department to have all soldiers in the best possible health before going to theaters of operation, General Davis said, would keep to the lowest possible level the number who would eventually have to be treated in general hospitals; that view is corroborated in the present low disease rate not only in the homeland but in the actual theaters of operation.

WALTER REED HOSPITAL'S CONVALESCENT CENTER

A convalescent center for Walter Reed General Hospital has been opened in the buildings which were formerly the National Park College, a school for girls at Forest Glen, Md. The convalescent unit provides an additional 1,150 beds, bringing the total capacity of Walter Reed Hospital to 3,325 beds. Careful planning has resulted in the fullest use of the facilities of the girls' school, located in beautiful park grounds which provide extensive recreational facilities, a swimming pool, bowling alley, amusement hall, gymnasium and walks and drives through shady groves. The excellent chapel contains a pipe organ and two libraries for patients. The clinic facilities for physical therapy, occupational therapy and dental work are extensive. The commanding officer at Walter Reed General Hospital is Brig. Gen. Shelly U. Marietta, Assistant Surgeon General, who is also in command of the Army Medical Center. General Marietta has had a distinguished administrative and professional career dating back to 1910, when he first entered the military service.

MALARIA RECONNAISSANCE AND COMBAT UNITS

According to the *Army and Navy Journal*, the War Department reports that the medical department has established sixteen "reconnaissance" units and twenty-six "combat" units to control the spread of malaria. The "reconnaissance" units are engaged in survey activities, each unit consisting of a parasitologist, four technicians, four field collectors and three chauffeurs. Each "combat" unit has a malaria engineer, eight noncommissioned officers and privates and three chauffeurs. The forty-two malaria control units are, or soon will be, in operation in areas where malaria is prevalent. The War Department reported that remarkably few fatalities have been attributed to malaria to date, owing largely to the antimalaria instructions, equipment and treatment available to troops.

THE HAMMOND GENERAL HOSPITAL

The new U. S. Army Hammond General Hospital near Modesto, Calif., will eventually have a capacity of 2,000 beds. It is of the cantonment type and is equipped to give treatment in all types of cases admitted to a general hospital. Recently it was designated by the War Department as a hospital which will receive also patients requiring special chest surgery (THE JOURNAL, March 27, p. 1095).

The hospital was named in honor of Brig. Gen. William H. Hammond, a pioneer in the development of medical field service and field hospitalization and a Surgeon General of the army during the Civil War.

The commanding officer of the Hammond General Hospital is Col. Luther R. Poust, M. C., and the executive officer Lieut. Col. U. R. Merikangas, M. C. The chiefs of service now on duty are:

Medical Service: Major Garnett Cheney, associate professor of clinical medicine, Stanford University School of Medicine, Stanford University, Calif.

Surgical Service: Major George S. Reynolds, on the staff of House of Mercy Hospital and St. Luke's Hospital, Pittsfield, Mass.

Neuropsychiatric Service: Lieut. Col. Mark Zeifert, chief of psychiatric service, Brooklyn Hospital, Brooklyn.

Eye, Ear, Nose and Throat Service: Major Alfred Wachsberger, adjunct professor of otolaryngology, New York Polyclinic; adjunct otolaryngologist Beth Israel Hospital, New York.

Outpatient Service: Major Ralph E. Pray, on the staff of Monterey County Hospital, Salinas, Calif.

X-Ray Service: Major Marvin L. Napper, Staff, St. John's, Burge and Springfield (Mo.) Baptist hospitals.

Laboratory Service: Captain Russell Kerr, pathologist, Kansas City, Mo.

The other medical officers assigned to this hospital and their previous locations are:

Major William M. Askew Jr., hospital inspector, Auburn, Ala., and Capt. H. F. Nachtman, registrar, resident, University of Pennsylvania Graduate School, Philadelphia.

Medical Service: Major Benjamin Rubin, South River, N. J.; Capt. Peter Callahan, Philadelphia; Capt. Edward Denenholz, director of maternal and child welfare, department of health, Chicago; Capt. F. R. Maddison, Tacoma, Wash.; Capt. Richard L. Saunders, dermatologist and syphilologist, Buffalo; Lieut. Vincent Bellafiore, Brooklyn; Lieut. C. C. Greene Jr., intern, Jefferson Medical College Hospital, Philadelphia; Lieut. Sidney Margulis, resident, Edward J. Myer Memorial Hospital, Buffalo; Lieut. Murray May, dermatologist, matriculate at New York Hospital, New York; Lieut. Morris McFarland, Lahey Clinic, Boston, and Lieut. Aaron Spirer, New York.

Surgical Service: Major Dolan E. Hodges, urologist, Billings, Mont.; Major Eurfryn Jones, Camp Hill, Pa.; Major Manuel Pusitz, orthopedic surgeon, Kansas Crippled Children's Commission and Capper Foundation for Crippled Children, Topeka, Kan.; Major Hilen K. Wallace, St. Joseph, Mo.; Capt. Edward Jones, resident in urology, Grady Hospital, Atlanta, Ga.; Capt. Allen Lilienthal, Memphis, Tenn. Capt. Arnold Naegeli, St. Paul, Minn.; Capt. Carlton Price, obstetrician and gynecologist, Rochester, N. Y.; Lieut. Eli Bernstein, surgeon, Flint, Mich.; Lieut. J. F. Bolkovatz, Fresno, Calif.; Lieut. E. Davis, Vincentown, N. J., on staff of Cooper Hospital, Camden, N. J.; Lieut. Abraham Klein, New York; Lieut. Frederick Luger, on staff of St. Mary's Hospital, Saginaw, Mich., and Lieut. Harold B. Miles, resident in anesthesia, Methodist Hospital, Indianapolis.

Neuropsychiatric Service: Capt. H. B. Hargus, medical director, Twin Pines Sanitarium, Belmont, Calif.; Psychiatrist, San Mateo County Hospital, San Mateo, Calif.; Capt. W. L. Noe, Lanhorne, Pa.; on staff of Abington (Pa.) Memorial Hospital; Lieut. Roger Dixon, administrative psychiatry, Elwyn (Pa.) Training School, and Lieut. E. R. Miller, Mercy Hospital, San Diego, Calif.

Eye, Ear, Nose and Throat Service: Capt. N. H. Battles, on staff of Latter Day Saints Hospital and Idaho Falls Sacred Heart Hospital, Idaho Falls, Idaho; Capt. Michael Lewin, plastic surgeon, on staff of Sydenham and Mount Sinai hospitals, N. Y., and Capt. James E. Reeder, on staff of Lutheran Hospital, Sioux City, Iowa.

NAVY

MEDICAL SPECIALISTS UNIT NO. 110

Naval Medical Specialists Unit No. 110, organized at the Cleveland Clinic (Ohio), reported for duty at the Naval Medical Supply Depot in Brooklyn in March 1942 in connection with the establishment of Naval Mobile Hospital No. 4 of several hundred beds which could be set up in a short time on arrival overseas. The material included seventy prefabricated metal buildings, equipment and supplies for the numerous departments of a hospital, even fire fighting apparatus, laundry, power and light, refrigeration and water supply. The personnel was to comprise about 20 medical and dental officers and 180 enlisted men. The original complement of officers from Cleveland comprised Lieut. Comdr. J. R. Kennedy, ophthalmologist and otolaryngologist; Lieut. Comdr. J. C. Root, roentgenologist; Lieut. Comdr. A. C. Ernstene, internist; Lieut. Comdr. W. James Gardner, neurologic surgeon; Lieut. Comdr. W. J. Engel, urologist; Lieut. Comdr. D. H. Nichols, dentist; Lieut. George Crile Jr., surgeon; Lieut. Guy H. Williams Jr., psychiatrist, and Lieut. (jg) E. J. Ryan, clinical pathologist. While waiting for the hospital to be assembled before embarkation the following additional medical officers, several of whom had taken postgraduate training in Cleveland, arrived: Lieut. Hays R. Yandell, Lieut. Gordon Sinclair, Lieut. Ray Andrews, Lieut. Ralph Zupanek, Lieut. (jg) George Berry (D.C.), Lieut. Charles Bingham, Lieut. Comdr. Dennis O'Connor, Lieut. (jg) Royston Miller, Lieut. Burnell Eckart, Lieut. Comdr. Russell H. Blood and Lieut. (jg) Fred Sanborn.

The commanding officer, Capt. John H. Robbins, M. C., U. S. Navy, and Lieut. Comdr. W. James Gardner, M. C., U. S. Naval Reserve, were detached from the unit and sent to New Zealand to make preliminary arrangements for the establishment of the hospital. Lieut. Comdr. Gardner describes the trip across the Pacific in the Bulletin of the Academy of Medicine of Cleveland and the environment in which the hospital was eventually established. The site selected was a hockey field of several acres about 3 miles from Wellington. The setting up of this hospital in a new country, he says, was a remarkable accomplishment, done largely by untrained hands, but in one month from the day work started the wards, operating rooms, mess halls and x-ray department were ready to function, and on that day 366 casualties were received from the landing operations in the Solomons. Within two months the hospital had received more than 1,200 wounded, of whom only 1 died. The hospital was then enlarged to 1,000 beds by adding wards built of New Zealand materials and by local labor. The complement of medical officers on the staff then was doubled. Lieutenant Commander Gardner in the fall returned to San Francisco with a large group of the wounded and later, he says, was transferred to inactive duty. When he left the outfit in Wellington, all the men were in excellent health.

EPIDEMIC CONTROL SPECIALISTS

Thirty-four officers and fifty-eight hospital corpsmen were graduated on April 3 as epidemiologists in a ceremony held at the National Naval Medical Center, Bethesda, Md. The graduates were addressed by Rear Admiral Luther Sheldon Jr., assistant chief of the Bureau of Medicine and Surgery. These doctors, technical specialists and enlisted men have been divided into epidemiologic teams for assignment to naval stations, marine amphibious forces and overseas bases, where they will maintain sanitary conditions and guard against outbreaks of disease. Within the continental limits, these teams will be composed of two officers and four hospital corpsmen; in overseas activities the composition will vary, depending on local conditions and the character of the unit to which the team is attached. A new class will start training on April 19 at the Naval Medical School.

EXAMINATION FOR APPOINTMENTS IN THE NAVAL MEDICAL CORPS

The next examination for appointments as acting assistant surgeons for intern training and for assistant surgeons, United States Navy, will be held at all of the major naval hospitals on May 3 to 7 inclusive. To date more than two hundred applications have been approved for these examinations.

INSTRUCTION IN MALARIOLOGY

A class of six medical officers was convened at the Naval Medical Center, Bethesda, Md., on April 15 for a course of instruction in malariology; seventy-two members of the Naval Hospital Corps and H-V(S) officers will also be convened for instruction in malariology and epidemiology on the same date.

MISCELLANEOUS

MEDICAL ATTENDANTS FOR MERCHANT SHIPS

A new school has been established at the Sheepshead Bay Training Station of the War Shipping Administration for the intensive training of medical attendants to serve on merchant ships. The 250 men enrolled as apprentice seamen of the Maritime Service who graduated from the school on March 12 will rate as petty officers responsible to the ship's master for the handling of health and sanitary problems. The school, which is under the supervision of the U. S. Public Health Service and under the immediate charge of Dr. S. S. Heilweil, has a staff of instructors and nurses, laboratories, lecture halls, sound film projection and other equipment necessary for the three months intensive course on sanitation, disease prevention, personal hygiene, first aid, transportation of the sick and injured, nursing and elementary pharmacy. This plan is said to be the first to provide every merchant ship, including cargo freighters, with a seaman trained and equipped to handle sanitary and health problems on board. The course is limited to men between 18 and 25 years of age with high school education.

NYLON SURGICAL SUTURES

Nylon has proved to be a superior replacement for silk in surgical sutures, according to du Pont de Nemours and Company, Inc., and millions of feet of nylon monofilament that formerly went into tennis racquet strings and other things will replace silk this year in surgical sutures for the army and navy and civilian use. Nylon will not dry out and rot like the natural fiber and it has greater tensile strength than silk. The monofilaments are solid strands in contrast to silk sutures, which are made by twisting together a number of threads. The nylon sutures are noncapillary, and bacteria cannot travel through them as they sometimes do in braided material; furthermore, being smooth and solid, skin cannot grow into the interstices as it sometimes does in the interstices of silk sutures, causing irritation and other complications when the sutures are removed. Nylon can be used internally as well as externally.

PRIORITY FOR MATERIAL FOR PRODUCTION OF HEALTH SUPPLIES

Since adequate priorities assistance for materials for the manufacture of health supplies is now assigned by other means, preference rating order P-29, formerly used for this purpose, has been revoked by the War Production Board. The revocation includes all serially numbered copies of P-29 and is effective immediately.

P-29, issued in August 1941, was formerly used for priorities assistance to manufacture surgical and dental instruments, x-ray equipment, biologic products, medicinal chemicals and other commodities in the health supply field.

Application for priority assistance in obtaining controlled materials and other materials necessary to complete authorized production schedules under CMP should now be made on form CMP-4B. Application for chemicals, biologic products and other miscellaneous items should be filed on form PD-1A.

ARMY-NAVY E AWARDS

The Army-Navy E Production Award was presented to the employees to the Baxter Laboratories, Inc., Glenview, Ill., at the public school auditorium in that community, March 11. The Baxter Laboratories are well known manufacturers of intravenous solutions and blood plasma and serum equipment.

James King & Sons, Inc., New York City, were awarded the Army-Navy E at ceremonies in the auditorium of the new Halloran General Hospital at Willowbrook, Staten Island, New York, which is said to be the largest army hospital in the United States. The ceremony was presided over by Supreme Court Justice John H. McCooey of Brooklyn and was attended by army and navy officers and hundreds of the employees of the company, who were praised for the speed and efficient manner in which the hospital was built. E pins also were presented to employees of the company.

PUBLIC HEALTH UNDER HITLER

By a decree published in the Reichsgesetzblatt, the fuehrer has entrusted the German Red Cross (DRK) with the entire transport of the sick in the sphere of civilian health services. According to DNB of January 23, he has, moreover, ordered the reich health leader, Dr. Conti, to issue the executory regulations in conjunction with the fuehrer's delegate for medical and health services, Prof. Dr. Brandt. The new scheme, resulting from the fuehrer's decree and the reich health leader executory order, represents progress in the work of the health services. Numerous organizations have hitherto dealt with the transport of the sick, and their activities have not been sufficiently coordinated. This has often made a uniform control of the transport of sick persons difficult. In many places, especially in the country, this work has already been carried out exclusively by the DRK. Those organizations which are at present still engaged in the transport of the sick will now inform the DRK of their facilities for this work, which they will, on request, transfer to the DRK for a corresponding compensation fixed in accordance with the Reich Compensation Law (Reichsleitungsgesetz). Likewise, the personnel who have hitherto transported sick persons, while maintaining their present rights, must, on request, be made available for incorporation into the DRK. The DRK will immediately start setting up the DRK Transport of the Sick and will announce locally when it is going to take over the entire transport. Until then, the organizations at present engaged in the transport of the sick are to carry on. The DRK, however, may give them instructions. The new regulations do not affect the transport of the sick of the armed forces, the Waffen-SS, those parts of the police which are subordinated to the armed forces, the Reich Labor Service and the Todt Organization.

The Leipzig *Neueste Nachrichten* of Nov. 29, 1942 reports that Saxony holds a leading place among all districts with regard to health services in factories; for instance, the number of industrial doctors has risen from 90 to 600 since the beginning of the war. It is now recognized as necessary to provide the factory health wardens with the necessary technical knowledge. In the Kneipp, a health resort of Berggieschubel, courses lasting a fortnight have been held. Men and women from the most important industrial concerns are here taking part in the training and at the same time are guests with full rights to use all facilities of the spa. They get their knowledge from practical experience on their own body. Early in the morning they get their ablutions and compresses according to a plan of treatment ordered by the doctor, and as their training proceeds they help one another with their treatment. Then follow lectures and practical demonstrations, beginning with compresses for the chest and finally those for the whole body, ablutions, herb baths and other baths of all kinds. These factory health officials are not meant to give regular treatment but are rather expected to pass on their knowledge and, above all, to set an example by their own natural way of living and to educate their fellow workers in it.

According to the Krakauer *Zeitung* of Nov. 19, 1942, the German Hospital, which has been extended and reconstructed, has now been handed over to Dr. Wiggers. It consists of five departments: the department for internal diseases, the surgical department, the department for skin and venereal diseases, the gynecologic department and maternity post, and an x-ray department. These departments, with the exception of the department for skin and venereal diseases, also treat outpatients. All departments are under the direction of specialists. The maternity post is to be transferred to the municipal maternity hospital, where a special department for German women is to be opened. The German Hospital of Lwów will be extended by a children's hospital. The admission to the German Hospital is subject to the regulations issued by the general government. Only the reich German and German speaking volkdeutsche are admitted.

Radio Paris of February 11 reported that hospital train No. 528 arrived, February 10, at the Gare de Lyon, Paris, from Germany with 384 patients, who were sent to three different hospitals.

ORGANIZATION SECTION

OFFICIAL NOTES

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the Medical Department of the United States Army and the United States Navy are on the air each Saturday at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts are heard by transcription at 10:30 p. m. Saturdays over Station WMAQ. Unless otherwise indicated, each program is summarized by Dr. W. W. Bauer, Director, Bureau of Health Education.

The titles and guest speakers for the next four programs are as follows:

April 24. "Sharp Eyes."
Speaker, Lieut. Col. Harold C. Lueth,
Liaison Officer, Surgeon General's Office and A. M. A.
United States Army.

May 1. "Jungle Death."
Speaker, Brig. Gen. C. C. Hillman,
Chief of the Professional Services, Office of the Surgeon
General, United States Army.

May 8. "Drugs March to War."
Speaker, Dr. Austin E. Smith, Secretary,
Council on Pharmacy and Chemistry.

May 15. "High Air."

BEFORE THE DOCTOR COMES

The American Medical Association program on Radio Station WLS (890 kilocycles) entitled "Before the Doctor Comes" will be on the air every Thursday morning at 9:45 up to and including May 27. Mrs. June Merrill will interview Dr. W. W. Bauer, Director, Bureau of Health Education, or Dr. Austin E. Smith, Secretary, Council on Pharmacy and Chemistry, on common home health problems. The titles for the next four programs are:

April 22. "What to Do About Bad Bumps."
(Bauer.)

April 29. "What to Do About Bleeding."
(Bauer.)

May 6. "What to Do About Foreign Bodies in the Nose, Ears, Throat or Eyes."
(Smith.)

May 13. "Growing Pains."
(Bauer.)

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Change in Status.—H. R. 1857 has passed the House and Senate, providing for the appointment of female physicians and surgeons in the Medical Corps of the Army and Navy.

Bills Introduced.—S. 939, introduced by Senator Pepper, Florida, proposes a federal appropriation of $11,580,000 for each fiscal year to enable each state to establish, extend and improve services for educating physically handicapped children. The sums to be made available will be used in making payments to those states which have submitted and had approved by the United States Commissioner of Education plans for the services indicated. S. 983, introduced by Senator Bailey, North Carolina, would authorize such sums as may be necessary to provide for the training of nurses for the armed forces, governmental and civilian hospitals, health agencies and war industries, through grants to institutions providing such training. This bill is identical with H. R. 2326, introduced by Representative Bolton. Both bills were introduced at the suggestion of the Administrator of the Federal Security Agency. H. Res. 202, submitted by Representative Shafer, Michigan, will, if adopted, direct the House Committee on World War Veterans' Legislation to make a survey of existing veterans' and military hospital facilities and a survey of the needs arising, and likely to arise, from the existing emergency for medical, tuberculosis and mental hospitals for veterans. The committee will be directed to submit to the House of Representatives a report covering a general program, with estimates of the cost, for the provision of hospital facilities likely to be needed. H. R. 2383, introduced by Representative Chapman, Kentucky, proposes to amend the Insecticide Act so as to provide that any white powder insecticide or fungicide containing arsenic in its elemental form or in any of its combinations, or fluorine in any of its combinations, shall, unless deemed unnecessary by the Secretary of Agriculture for the protection of the public health, be deemed to be adulterated unless it is distinctly colored in accordance with regulations promulgated by the Secretary of Agriculture. H. R. 2442, introduced by Representative Sparkman, Alabama, provides that during the present emergency and for six months thereafter the Chief of the Dental Division, Surgeon General's Office, Army of the United States, shall have the rank, pay and allowances of major general. The bill provides too that there shall be officers of the Dental Corps promoted to the grade of brigadier general at the ratio of one for each six officers of the Medical Corps promoted to like grade.

STATE MEDICAL LEGISLATION

California

Bills Introduced.—A. 686, to amend the Health and Safety Code, proposes, among other things, that the state director of health shall be a doctor of medicine eligible to license to practice in California, with at least one year's postgraduate training in public health and a minimum of five years' practical experience as an administrative officer in a well organized health department. A. 1335, to amend the law relating to the use and sale of poisons, proposes, among other things, to add the following poisons to schedule C 1: acetylurea, sulfonated methanes, paraldehyde, sulfanilamide except in tablets of 30 grains or more designed for stock purposes only and so labeled, sobisminol, amidopyrine, cinchophen, ergot, diethylstilbestrol, provided that they may be sold only at retail on order or prescription of a physician, dentist, chiropodist or veterinary surgeon duly licensed to practice in the state of California and shall not be refilled without order of the prescriber; to schedule C 2: amphetamine, thyroid, phenylhydantoin or their compounds, provided they are sold only at retail on the written order or prescription of a physician and surgeon, dentist, chiropodist or veterinary surgeon licensed to practice in the state of California but such prescription may be refilled for the person for whom originally written.

Colorado

Bills Enacted.—H. 199 was approved, March 31. To amend the chiropractic law, it requires chiropractors, at the time of the annual renewal of their licenses, to present proof that they have attended at least three days of a scientific clinic, forum or educational study approved by the Colorado state board of

chiropractic examiners. H. 200 was approved, March 31. It authorizes the chiropractic board to adopt a schedule of minimum educational requirements for chiropractic schools to be not less than 3,600 sixty minute hours of classroom instruction with a maximum of thirty hours per week.

Connecticut

Bills Introduced—Sub. for S. 562 proposes to authorize a town board of education to appoint one or more legally qualified practitioners of medicine as school medical advisers and to provide such medical advisers with adequate facilities to provide for private health examinations of individual pupils. H. 1194, to authorize a town health officer to detain and examine persons reasonably suspected of being infected with a venereal disease, has had an amendment to it introduced which would provide that nothing therein should be construed to interfere with the freedom of any adherent of the teachings of a well recognized religious sect, denomination or organization to depend exclusively on prayer for healing in accordance with the teachings of such sect, denomination or organization.

Georgia

Bill Introduced.—S. 213 proposes to require the secretary of state to issue licenses to practice naturopathy in Georgia to all persons who have been engaged in such practice in Georgia for the past three years and who have a license so to practice in the state of South Carolina. This proposal died in the Senate.

Bills Enacted.—H. 136 has become Governor's Act No. 346 of the Laws of 1943. It requires all licensed physicians attending a pregnant woman to take a sample of blood within thirty days of the first examination and to submit such sample to an approved laboratory for a serologic test for syphilis. The title to this bill indicates that the word "physician" wherever used in the act shall be construed to embrace and include those persons licensed to practice under the osteopathic laws of Georgia. H. 552 has become Governor's Act No. 462 of the Laws of 1943. It abolishes the state boards of medical examiners, chiropractic examiners and osteopathic examiners and creates in their stead a State Commission of Medical Examiners, Georgia Commission of Chiropractic Examiners and State Commission of Osteopathic Examiners of Georgia. The powers, duties and qualifications of the new commissions are the same as those of the prior boards except that members thereof appointed by the governor must be approved by the secretary of state and confirmed by the senate.

Illinois

Bills Introduced.—S. 244 and H. 393 propose to provide for the establishment and maintenance of county and multiple county public health departments. H. 370, to amend the unemployment compensation act, proposes that an employee will not be ineligible for benefits if he is unable to work because he is sick and has submitted proof of such sickness by means of a statement by a duly licensed physician. H. 390 proposes to authorize the department of registration and education to issue licenses to practice physio-therapy, defined as the method, art or science of treating the human body for hygienic or remedial purposes by the following methods: massage and manipulations with the hands or with any other physiotherapy modality, and the use of such adjuncts as light, heat, air, water, diet, gymnastics and electricity. H. 395 proposes to authorize any town or two or more adjacent towns to be organized into a public health district.

Iowa

Bills Introduced.—S. 370, to amend the premarital examination law, proposes to permit a licensed physician who is a member of the armed forces of the United States, and authorized to make tests and examinations for syphilis to execute the required certificate for an applicant who is likewise in the armed forces. S. 371, to amend S. 82, concerning the income tax law, which was approved by the governor March 11, 1943, proposes that a taxpayer may deduct expenses paid during the taxable year, not compensated for by insurance or otherwise, for medical care of himself, his spouse or any dependents. The term "medical care" is defined to include amounts paid for the diagnosis, cure, mitigation, treatment or prevention of disease or for the purpose of affecting any structure or function of the body and also treatment or nursing as prescribed by a well recognized church or religious denomination in any hospital or at home or in a sanatorium conducted and operated by such church or denomination.

Maine

Bill Passed.—H. 1352 passed the senate, April 5. To amend the law relating to infectious and communicable diseases, it proposes that every physician shall, within forty-eight hours of the time the fact comes to his knowledge, report in writing to the state bureau of health any person known by said physician to have any of the following infectious and communicable diseases: syphilis, gonorrhea, chancroid and lymphogranuloma venereum. The proposal would also authorize the state bureau of health to detain and examine any person believed to be infected with one of the aforementioned diseases and so conducting himself as to expose others to the dangers thereof.

Bills Enacted.—S. 457 became chapter 236 of the Laws of 1943. It amends the act relating to procuring or attempting to procure an abortion or miscarriage by exempting therefrom those instances in which the abortion or miscarriage is necessary for the preservation of the mother's life. H. 328 has become chapter 273 of the Laws of 1943. It authorizes the state board of registration of medicine to issue temporary emergency certificates, by general regulations or specific orders, to such physicians, licensed outside the state, as it shall find qualified to practice in the state of Maine during the emergency period, for the time specified in the temporary license and in the area limited thereby. H. 1202 has become chapter 195 of the Laws of 1943. It authorizes cities and towns to raise money for the purpose of subsidizing a physician to induce him or her to settle in said town.

Massachusetts

Bills Introduced.—H. 727 proposes to authorize a physician registered under the general laws to furnish contraceptives to a married woman in any case in which, after diagnosis, such physician is of opinion that her health or life would be endangered by pregnancy. H. 1462, appendix H, to amend the narcotic drug law, proposes to add marihuana to the list of drugs covered by the law.

Minnesota

Bill Introduced.—H. 1361 and S. 1230, to amend the basic science law, proposes that during the war and while accredited medical schools are accelerating their courses, the board of examiners may give examinations to applicants who are registered students in an accredited medical school and who are otherwise qualified even though such applicant is not 21 years of age.

Bill Enacted.—S. 825 has become chapter 314 of the Laws of 1943. To amend the law relating to coroners, it provides that any coroner or deputy coroner who is a duly licensed and registered physician and surgeon shall not be disqualified from rendering medical care or hospitalization to a recipient of public relief, from being appointed an examiner in insanity or incompetency hearings or from being compensated therefor.

Missouri

Bill Introduced.—H. 85, proposing to define the words physician and surgeon so as to include osteopaths and to authorize such persons to practice in government supported hospitals, was amended in the house so as to provide that the right to practice in such hospitals would devolve on and be enjoyed by only such practitioners as have acquired education, experience and training of a standard equivalent to that required by the board of trustees of the hospital.

Nebraska

Bill Enacted.—Bill No. 149 was approved, March 29. It exempts from the payment of the annual renewal license fee chiropractors, osteopaths and physicians while actively engaged in the military service of the United States as defined in the Soldiers' and Sailors' Civil Relief Act.

New Hampshire

Bill Passed.—H. 267, as amended by the house committee, passed the house, March 30. It proposes the licensing of physiotherapists who have been engaged in the practice of physiotherapy for at least one year prior to the passage of the act.

New Jersey

Bills Passed.—S. 68 and S. 72 passed the senate, March 30. Both proposals would exempt from a law requiring compulsory vaccination for smallpox and diphtheria those persons who present an affidavit that vaccination violates a tenet of the established religious society, institution, organization or sect of which he is a member. A. 276 passed the house, April 1. To amend the medical practice act, it proposes to exempt from the provisions thereof chiropodists while operating under the specific direction of a regularly licensed physician or surgeon.

New Mexico

Bill Introduced.—Senate substitute for S. 141 proposes that every physician who makes a diagnosis of or treats or prescribes for a case of venereal disease shall report such case immediately to the municipal or district health officer and authorizes state, district and municipal health officers to detain and examine persons reasonably suspected of being infected with a venereal disease and to require persons so infected to report for treatment to a reputable physician.

New York

Bills Enacted.—C. C. H. S. 16, adopted, March 20, enacts a resolution to the effect that a legislative committee be appointed to make a comprehensive and thorough study of legislation enacted in other states for the regulation, control and licensing of chiropractors, to determine proper educational standards and requirements, and to prepare and recommend legislation for the regulation and licensing of chiropractors in New York. A. 335 has become chapter 294 of the Laws of 1943. It authorizes the state commissioner of health to employ necessary medical and health personnel for rendering services in areas designated by the governor as being emergency health and sanitation areas by virtue of an inadequacy of medical facilities or personnel therein. Compensation to such employed medical personnel may be paid by the state department of health. A. 1125 has become chapter 193 of the Laws of 1943. It amends the medical practice act by postponing until July 1, 1944 the 1942 amendment exempting students, interns and resident physicians from the operation of such act.

North Dakota

Bills Enacted.—S. 77 was approved, March 20. It provides for the establishment, maintenance and duties of a district board of health and provides that the district health officer appointed by such board shall be a physician and surgeon regularly licensed to practice medicine and surgery in the state of North Dakota. H. 229 was approved, March 12. It provides for the organization and regulation of nonprofit hospital service plan corporations.

Ohio

Bills Introduced.—S. 237 proposes to provide a comprehensive program for the physical rehabilitation of war veterans. H. 345 proposes the creation of a state board of chiropractic examiners. Chiropractic is not defined by the proposal, but the bill would prohibit a chiropractor from practicing major surgery or obstetrics or administering general anesthetics until he shall have passed an examination in those subjects given by the state medical boards.

Bill Passed.—Substitute for H. 112 passed the house, March 30. It proposes to amend the law relating to osteopaths by providing for one osteopathic member of the medical examining board and requiring osteopaths to be examined by such board in the subjects of anatomy, physiology, pathology, chemistry, and diagnosis, surgery, obstetrics and such other subjects as the board requires and by the osteopathic member in the subjects of materia medica and therapeutics and the principles and practice of osteopathic medicine. Successful applicants would be entitled to practice osteopathy and surgery. Persons now licensed to practice osteopathy but who have not passed an examination before the state medical board would be allowed to continue to practice osteopathy and minor and orthopedic surgery but not to practice major surgery.

Oklahoma

Bill Enacted.—H. 222 was approved, March 24. It amends the medical practice act by providing, among other things, that the members of the board of examiners must be citizens.

Oregon

Bills Enacted.—S. 284 was approved, March 29. It authorizes the payment of workmen's compensation to employees disabled by an occupational disease defined as (1) any disease or infection which is peculiar to the industrial process in which the employee is engaged and which arises out of and in the scope of the employment, and to which the employee is not ordinarily subjected or exposed other than during a period of regular actual employment, (2) silicosis—meaning a disease of the lungs caused by breathing silica dust (silicon dioxide) producing fibrous nodules, distributed through the lungs and demonstrated by x-ray examination or by autopsy. H. 229 has become chapter 402 of the Laws of 1943. It reenacts and extends the existing law providing for state reimbursement to hospitals for services rendered victims of motor vehicle accidents so as to cover nurses, doctors and owners and operators of ambulances as well. H. 350 has become chapter 218 of the Laws of 1943. It authorizes commissioned medical officers of the army to execute the certificate necessary under the state premarital examination law.

Pennsylvania

Bills Introduced.—S. 209, to amend the osteopathic law, proposes, among other things, to require the board of examiners, by inspection or otherwise, to examine and fix the rating of all colleges and hospitals outside the state whose graduates or interns desire to obtain osteopathic licensure in Pennsylvania. S. 460 proposes the creation of a state board of naturopathic education and licensure and defines naturopathy as a system of treatment and prevention of body ills without the use of drugs or surgery, including in its armamentarium such natural elements as air, light, heat, electricity, water, phytotherapy, diet and/or physiologic and psychologic dysfunctions of the human body, provided that nothing in the proposal would be held or construed to authorize any naturopathic physician licensed thereunder to use drugs or surgery. H. Res. 45 proposes a resolution to the effect that the department of health should initiate a campaign of education in order to bring home to the people the advisability and necessity of new immunization against disease and that the department through its county boards should make available sufficient serums and vaccines to properly guard the people against disease. H. 669, to amend the law regulating and supervising nonprofit medical service corporations, proposes that subscribers earning more than a certain specified sum shall be liable to doctors of medicine registered with the corporation and rendering services to such persons for the full amount of the usual fees and charges for such services made by doctors of medicine, and any payment made by the corporation to doctors for rendering such services shall be a payment on account and not necessarily in full. H. 673, to amend the law relating to occupational diseases, proposes to include within the meaning of the term "occupational disease" infection or inflammation due to bacterial or parasitic agents in any occupation involving direct contact with or exposure to such agents. H. 893 proposes the creation of a state board of chiropractic examiners and defines chiropractic as the science of treating human ailments by manipulation and adjustment of the spine of the human body and adjacent tissues thereof and the use of such mechanical, physiotherapeutic, dietetic, hygienic and sanitary measures, except drugs and surgery, as are incident to the care of the human body, as taught and practiced in approved schools and colleges of chiropractic.

Bill Enacted.—H. 236 has become act No. 8 of the Acts of 1943. It provides that for the duration of the war a minimum of nine months rather than one year internship shall constitute the necessary training to qualify for admission to examination for a license to practice medicine.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Acting Health Officer of Los Angeles County. — Dr. Hubert O. Swartout, director of the bureau of preventable disease in the Los Angeles County Health Department, has been appointed acting health officer of the county. Dr. Wilton L. Halverson, Sacramento, director of the department, was recently appointed in charge of the state department of health.

The George Dock Lecture. — The annual George Dock Lecture of the Barlow Society for the History of Medicine was delivered by Dr. George Blumer, David P. Smith clinical professor of medicine emeritus, Yale University School of Medicine, New Haven, April 2, at the Los Angeles County Medical Association. His subject was "Remarks on the Life and Accomplishments of William Heberden the Younger." The lecture marked the eighty-third birthday of Dr. Dock.

Lillien Jane Martin Dies.—Lillien Jane Martin, Ph.D., emeritus professor of psychology at Stanford University, died at her home in San Francisco, March 26, aged 91. Dr. Martin was born in Olean, N. Y., July 7, 1851, receiving an honorary doctor of philosophy degree from the University of Bonn in 1913. She was a member of the department of psychology at Stanford from 1899 to 1916, when she became emeritus professor. Consulting psychologist in San Francisco and psychopathologist and chief of the mental hygiene clinic at the San Francisco Polyclinic and Mount Zion Hospital since 1916, Dr. Martin was founder and director of the Old Age Center in San Francisco and president of the California Society of Mental Hygiene from 1917 to 1921. The New York *Times* credits Dr. Martin with being the founder of the first child guidance clinic in the country. She was a member of many scientific societies and the author of extensive writings in her specialty.

State Medical Meeting.—The seventy-second annual session of the California Medical Association will be held at the Biltmore Hotel, Los Angeles, May 2-3, under the presidency of Dr. William R. Molony Sr., Los Angeles. Among the out of state speakers will be:

Dr. John H. Fitzgibbon, Portland, Ore., Wartime Community Health Problems in Oregon.
John R. Mannix, Detroit, director, Michigan Hospital Service, Voluntary Nonprofit Health Plans.
Dr. Tom D. Spies, Cincinnati, and Birmingham, Ala., Detailed Methods of Diagnosis and Therapy in Acute Nutritive Failure.
Dr. William A. Sawyer, Rochester, N. Y., Some Medical Problems in Wartime Industry.
Philip Drinker, Chem.E., Washington, D. C., Health Control in Welding Work.
Dr. John H. Hutton, Portland, Spinal Anesthetic Agents and Methods Usually Employed at the University of Oregon Medical School Hospitals.
Lieut. H. L. Gartshore, M. C., Army of the United States, Pendleton, Ore., Psychiatry at an Air Base Station Hospital.

The program also includes a wide range of subjects to be presented by military and civilian physicians.

CONNECTICUT

Premarital Blood Test Law Amended.—Out of state physicians and osteopaths are now eligible to sign marriage applications in Connecticut under a bill signed by the governor March 18. The act permits any physicians or osteopaths duly licensed in any state or territory of the United States or in the District of Columbia to sign a statement for marriage license application in Connecticut. According to the state department of health, the action is expected to relieve present difficulties, particularly on the part of men in the armed forces who are stationed in various sections of the country and desire to be married in Connecticut.

The Yale Poliomyelitis Study Unit. — The National Foundation for Infantile Paralysis has made a five year grant totaling $150,000 to Yale University School of Medicine, New Haven, to establish the Yale Poliomyelitis Study Unit. The term of the grant will conclude on June 30, 1948. In 1941 the Yale Poliomyelitis Commission was established by Drs. James D. Trask (now deceased) and John R. Paul, New Haven, as a result of problems which grew out of the epidemic which swept New England that year. The commission's aim has been to develop a virus laboratory adapted for use by clinical members investigating the methods by which the disease is transmitted. The school of medicine will reorganize its investigation of poliomyelitis problems. Henceforth studies will be conducted in the Poliomyelitis Study Unit under the direction of Dr. Paul, professor of preventive medicine, who will have administrative direction of the unit. An advisory committee of the National Foundation will be appointed by Mr. Basil O'Connor, New York, president, to consult with Dr. Paul and his associates as the need arises. As far as facilities permit, the foundation may send to the unit individuals properly qualified in the opinion of the foundation's medical advisory committee, to pursue definite lines of investigation. To meet the immediate needs of the study unit space will be arranged by the Yale University School of Medicine. None of the funds granted by the National Foundation for Infantile Paralysis will be used for the construction of new buildings.

Lectures on Non-War Psychiatry.—A series of lectures was given recently at the Graduate Club of the Neuro-Psychiatric Institute of the Hartford Retreat, Hartford. The series was devoted exclusively to non-war neurology and non-war psychiatry:

Dr. Foster Kennedy, New York, (*a*) Neurological Examinations; (*b*) Gaits, the Midbrain, Hysteria; (*c*) Myotonia, Myasthenia and Other Neurological Conditions.
Wladimir T. Liberson, Hartford, Psychiatric Research in Electroencephalography.
Dr. Abraham A. Brill, New York, Various Schools of Psychotherapy.
Dr. Abraham Myerson, Boston, My Philosophy of Psychotherapy.
Dr. William Healy, Boston, Early Schizophrenic.
Douglas H. Fryer, Ph.D., New York, Research Observations in Preparatory Muscular Activity in Relation to Work.
Dr. Clarence B. Farrar, Toronto, An Editor Looks at the Psychiatric Literature.
Dr. Edward A. Strecker, Philadelphia, Alcoholism: "Something on Therapy in Alcoholic Conditions."
Dr. Charles Macfie Campbell, Boston, Common Sense in Psychiatry.
Dr. Harold G. Wolff, New York, Emotions and Disease.
Dr. Donald J. MacPherson, Boston, Relationship Between the Referring Man and the Mental Hospital.

FLORIDA

Graduate Department of Medicine Organized. — A department of medicine has been established in the Graduate School of the University of Florida, Gainesville. The new unit will be located in Jacksonville and maintained in cooperation with the state medical association and the state board of health. Dr. Turner Z. Cason, Jacksonville, will be in general charge as director of the department. The new unit, which will conduct graduate courses and promote research in medicine and surgery, is the outgrowth of the annual graduate short course for doctors of medicine inaugurated about ten years ago. Continuation courses for practicing physicians with facilities for clinical instruction will be given from time to time.

ILLINOIS

Dr. Brokaw Named Acting Director of Health District.—Dr. Raymond V. Brokaw, Springfield, chief of the division of cancer control, state department of public health, has been named acting director of the Champaign-Urbana Public Health District, effective March 16. He has succeeded Reuben F. Reider, Champaign, passed assistant surgeon, U. S. Public Health Service Reserve. According to the Illinois Department of Public Health, this is an unprecedented action by the state to share with a local health office the services of a division chief.

Chicago

Billings Lecture.—The Institute of Medicine of Chicago announces that Carl Voegtlin, Ph.D., chief of the National Cancer Institute, Bethesda, Md., will deliver the fifth Frank Billings Lecture of the Thomas Lewis Gilmer Foundation at the Palmer House, May 28. His subject will be "Chemistry of Carcinogenesis and Tumor Growth."

Mental Hygiene Meeting.—Dr. Davis Slight, professor of psychiatry, University of Chicago, was reelected president of the Illinois Society for Mental Hygiene at its thirty-fourth annual meeting in Chicago, March 15. William B. Basile, lawyer, is secretary. Harold G. Webster, Detroit, executive secretary of the Michigan Society for Mental Hygiene, addressed the meeting on "Strategy and Tactics in Mental Hygiene."

INDIANA

Hospital Ward Named for Physician. — A forty bed obstetric ward at the Indianapolis City Hospital was dedicated and named, March 23, in honor of Dr. Henry F. Beckman, Indianapolis, who has been in charge of the obstetric service at the hospital for more than thirty years. A bronze plaque was unveiled in the ward by Dr. Charles W. Myers, medical superintendent of the hospital, as a feature of the dedication to Dr. Beckman. Another feature of the occasion was a talk by Sister Elizabeth Kenny.

MARYLAND

Annual Medical and Chirurgical Faculty Meeting.—The annual meeting of the Medical and Chirurgical Faculty of the State of Maryland will be held in Baltimore, April 27-28. Dr. Charles R. Austrian, Baltimore, president of the faculty, will deliver the presidential address on "Plans for Medical Care." Dr. Frank L. Horsfall Jr., New York, will present the Trimble Lecture on "Primary Atypical Pneumonia." Included on the program will be the following Baltimore physicians:

Dr. Marcus M. Ravitch, Preparation and Uses of Frozen and Dried Plasma.
Dr. Warfield M. Firor, Tetanus and Gas Infections.
Dr. Otto C. Brantigan, Compression Treatment of Burns.
Dr. James G. Arnold Jr., Management of Acute Head Injuries.
Dr. Charles A. Reifschneider, Intra-Abdominal Injuries.
Dr. Warde B. Allen, Cardiac Problems in Aviation.

One session will be devoted to "The Distribution and Redistribution of Physicians in the United States." Dr. Arthur M. Shipley, Baltimore, will be chairman of the discussion, and speakers will be Dr. Harvey B. Stone, Baltimore, and Brig. Gen. George F. Lull, M. C., U. S. Army, Washington, D. C. Twenty-four subjects will be covered in the round table discussion at the Belvedere Hotel, April 28.

MASSACHUSETTS

The Cutter Lecture on Preventive Medicine.—Dr. Lowell T. Coggeshall, professor of epidemiology, University of Michigan School of Public Health, Ann Arbor, Mich., will deliver the Cutter Lecture on preventive medicine, April 27, at Harvard Medical School on "Importance of Tropical Diseases in the Current and Post War Period."

Fiftieth Anniversary of Tufts Medical School.—September has been tentatively selected as the month to mark the fiftieth anniversary of Tufts College Medical School, Boston. The nature of the celebration will be appropriate to the wartime exigencies and preoccupations of those concerned when the time approaches. A committee has been appointed to develop plans and arrangements for the observance.

MISSISSIPPI

Student Loan Fund.—A gift of $2,500, with a similar amount to be added in 1944, to the University of Mississippi School of Medicine, University, for the establishment of the G. D. Shands Memorial Loan Fund for medical students has been received from Paul Hill Saunders, Ph.D., and his wife of New Orleans and New York, newspapers reported March 14. The fund was presented in memory of the late Gov. Garvin D. Shands, Mrs. Saunders' father and for many years dean of the university school of law. It will be made available to worthy students who complete the two year course offered by the university and who need financial aid to finish their medical training at other schools.

NEVADA

Annual Registration Due May 1.—All persons holding licenses to practice medicine in Nevada are required by law to pay annually to the treasurer of the Board of Medical Examiners, on or before May 1, a tax of $2. Failure to do so operates to forfeit a licentiate's right to practice medicine, and his license to practice can be reinstated thereafter only on payment of a $10 penalty.

NEW YORK

Outbreak of Sore Throat.—An outbreak of 56 cases of sore throat early in March in a village in Saratoga County has been traced to the consumption of raw milk. *Health News* reports that, although the epidemiologic investigation has not been completed, it is estimated that on the basis of the number of consumers of the suspected milk a total of 130 persons were affected. The illness was characterized by acute onset, severe sore throat with considerable purulent exudate, enlarged cervical glands and, frequently, generalized symptoms including chills, fever and considerable prostration. The attack rate among persons drinking the incriminated milk was 36.4 per cent for those under 15 years of age and 44.1 per cent for those over 15 years. The health officer suspected an outbreak when 5 cases of sore throat, with onsets within a three day period, occurred in his practice. A house to house survey of a portion of the village showed that there were 34 cases among 79 consumers of milk from the implicated dairy and no cases among 55 consumers of milk from other dairies. Pasteurization of the suspected supply was instituted immediately, and no additional cases were reported with onsets occurring more than forty-eight hours after pasteurization was begun.

New York City

Symposium on the Premature Infant.—The Zeta chapter of Phi Delta Epsilon fraternity at Long Island College of Medicine, Brooklyn, announces a symposium with Dr. Sam Z. Levine, professor of pediatrics, Cornell University Medical College, New York, speaking on "The Handicaps of the Premature Infant." The discussion will be carried out by Drs. Charles A. Weymuller and Murray B. Gordon, professor of pediatrics and professor of clinical pediatrics, respectively, Long Island College of Medicine. The symposium will be presented at Hoagland Hall, Brooklyn, April 20.

NORTH CAROLINA

Tuberculosis Meeting Canceled.—At a recent meeting of the North Carolina Tuberculosis Association in Raleigh the executive committee voted to dispense with the usual annual meeting. Business matters will be settled at a meeting of the board of directors, the time to be announced later.

Venereal Disease Education Institute.—Announcement is made of the recent establishment in Raleigh of the Venereal Disease Education Institute, which is supervised by Mr. Capus M. Waynick, newspaper editor, High Point, and by the state board of health, to disseminate educational material on venereal diseases. The institute is operated by the U. S. Public Health Service and the Zachary Smith Reynolds Foundation, which has been supporting public health work in North Carolina for many years.

OHIO

Use of Radio for Health Education.—The Institute for Education by Radio, sponsored by Ohio State University, will devote a section meeting to "The Use of Radio for Health Education" at the Deshler-Wallick Hotel, Columbus, May 1, under the chairmanship of David Resnick, director of public relations, National Society for the Prevention of Blindness, New York. Speakers will include:

Sterling W. Fisher, assistant public service counselor and director of the Inter-American University of the Air, National Broadcasting Company, New York, The Role of the Broadcasting Industry in Health Education.
Dr. William W. Bauer, director, Bureau of Health Education, American Medical Association, Chicago, When Doctors Broadcast.
Daniel C. McCarthy, director of public relations, National Tuberculosis Association, New York, Selling Health by Radio.
Thomas C. Stowell, assistant director, division of public health education, New York State Department of Health, Albany, N. Y., Health on the Air Comes of Age in New York.

The Institute's annual conference will be held from April 30 to May 3.

Vesalius Exhibit.—In commemoration of the quartercentenary of the foundation of modern anatomy by Andreas Vesalius, an exhibit has been arranged in the Cleveland Medical Library. The exhibit was prepared by the staff of the Cleveland Branch of the Army Medical Library and the books are largely from its collections. Two important items from the collection of the Cleveland Medical Library, however, include a copy of the second edition of the Fabrica (1555), presented to the association in 1893 by Dr. Howard A. Kelly, who died in January 1943, and a copy of the first edition of the compendium of Geminus plagiarized from Vesalius in 1945. All the works of Vesalius are represented in the exhibit, though not in every case by first editions. Included in the exhibit are two copies of the Geminus compendium, London, 1545; the first edition of Fallopio's Observations, Venice, 1561; a copy of the attack on Vesalius by his former teacher Jacques Dubois (1551, represented by 1635 reprint); and a copy of the rare Murr reprint (1790) of the Christianismi restitutio of Servetus (1553), for which he was burned at the stake in Calvin's Geneva and which contains the earliest account of the pulmonary circulation, perhaps arrived at when he was fellow prosector of Vesalius at Paris about 1536.

TEXAS

Exhibit of Rare Medical Books.—A special exhibit of rare medical books from the collections of Chauncey D. Leake, Ph.D., dean and vice president of the University of Texas Medical Branch, Galveston, and of the medical school library was held at the University of Texas Library, Austin. At the opening of the exhibit Dr. Leake spoke to premedical students and faculty members on "The Medical Books of Fine Printers," illustrating his remarks with particular emphasis on the Fabrica of Andreas Vesalius, first published in Basel four hundred years ago.

GENERAL

Wartime Public Health Conference.—The American Public Health Association will sponsor a three day public health conference in New York, October 12-14. The seventy-second annual business meeting of the association will be held in connection with the conference, which will be devoted exclusively to wartime emergency problems as they affect public health and the public health profession. New York City was selected because more than 40 per cent of the association's membership is concentrated in and immediately around it.

Report of Menninger Foundation.—The first annual report of the Menninger Foundation, Topeka, Kan., covering the period April 1941 to July 1942, has been received. Work was carried out during the first year of operation on education and treatment of neurotic children, hypnosis, occupational therapy and psychoanalytic training and psychologic testing. At the recent annual meeting all the officers of the foundation were reelected including Drs. Karl A. Menninger, president, and William C. Menninger, secretary. An executive assistant, Jean Lyle Menninger, has been added to the staff to aid the secretary during his absence with the armed forces.

Chemist Awarded Prize for Research in Milk.—Earle O. Whittier, Chem.E., senior chemist of the bureau of dairy industry, U. S. Department of Agriculture, Washington, D. C., has been awarded the Borden Company Prize of $1,000 for research in chemistry of milk. The prize, which was to be presented April 14 at a meeting of the society in Detroit, is given in recognition of researches in the chemistry of milk constituents. Dr. Whittier received his degree as a chemical engineer at the University of Maine, Orono, in 1923. He had been a member of the teaching staff there from 1911 to 1915, when he went to Simmons College, Boston. From 1918 to 1921, when he joined the department of agriculture, he was research chemist at E. I. Du Pont de Nemours and Company.

Advisory Committee of Nutrition Foundation.—The Nutrition Foundation announces the following appointments to the food industries advisory committee: Franklin C. Bing, Ph.D., director, American Institute of Baking, Chicago; Edwin J. Cameron, Ph.D., director, Research Laboratories, National Canners Association, Washington, D. C.; Lillian B. Storms, nutrition research, Gerber Products Company, Fremont, Mich.; Carl Nordgren, research chemist, Chr. Hansen's Laboratory, Inc., Milwaukee; George C. Scott, M.S., director of research, Minnesota Valley Canning Company, Le Sueur; Louis E. Dietrich, director of production and research, P. Duff & Sons, Inc., Pittsburgh; Roland A. Morck, research department, R. B. Davis Company, Hoboken, N. J.; Arthur Weber, process superintendent, National Sugar Refining Company, New York, and C. G. Harrel, director of research, Pillsbury Flour Mills Company, Minneapolis. The advisory committee serves as a liaison group between the foundation and the food industry.

Conference to Consider Additions to Pharmacopeia.—A pharmacopeial open conference, dealing with the forthcoming first U. S. P. XII bound supplement, will be held at the Hotel Pennsylvania, New York, April 23-24. The major subject for discussion Friday evening will be the U. S. P. XII requirement that multiple dose packages of parenteral solutions be limited in size to ten average doses. An all day program Saturday will cover about one hundred revisions and other alterations in monographs now official in the U. S. P. XII. Following the open conference and a consideration of suggestions and discussions, the material will be printed as the first U. S. P. XII Bound Supplement. It was thought that this supplement would not be required for at least two years, but demands by war interests and the increased revision tempo have required so many changes and additions that its immediate publication became necessary. It will be distributed without further charge to all purchasers of the U. S. P. XII who mail in the order coupon found inside the back cover of the U. S. P. XII.

Medical Service Plans Meet in Chicago.—At a meeting of representatives of the various medical service plans, held in Chicago on February 14, it was agreed that an annual conference of representatives of such plans be held each year and that such a group form a council with president and secretary-treasurer. Dr. James C. McCann of Worcester, Mass., was elected president; Dr. Frank L. Feierabend of Kansas City, Mo., was elected secretary-treasurer. It was voted that a committee be appointed to act as a group to provide cooperation between the American Medical Association, the Canadian Medical Association and the new Medical Service Plans Council. The committee appointed consists of Drs. Chauncey L. Palmer of Pittsburgh, chairman, Jason A. Hannah of Toronto and Robert L. Novy of Detroit. Mr. Jack Laux, Detroit, of the Michigan plan was appointed research director. It was also agreed that a meeting of this group be held at the time of the meeting of the House of Delegates of the American Medical Association in Chicago. Kansas City, Mo., was selected as the national headquarters for the council, and an annual contribution of $25 was volunteered by each organization to pay the expenses of the function.

HAWAII

Island Health Activities.—William L. Zink, assistant surgeon, U. S. Public Health Service Reserve, has been assigned to operate the new mobile x-ray unit of the Territory of Hawaii health board.——Dr. Alfred S. Hartwell, Honolulu, has recently been named medical director for Queen's Hospital. A new building has been constructed at the hospital to house the Honolulu Blood Bank; funds were provided by the Office of Civilian Defense.——The Hawaii Territorial Society for Mental Hygiene was recently organized under the auspices of the Psychiatric Committee of the Hawaii Territorial Medical Association.——The name of Japanese Charity Hospital, Honolulu, has been changed to Kuakini Hospital.——Major Charles L. Wilbar Jr., M. C., U. S. Army, has been appointed health officer of Maui County with headquarters in Wailuku.

CANADA

First Social Hygiene Day.—On February 3 the first Canadian Social Hygiene Day was observed under the auspices of the Health League of Canada, according to the *Canadian Journal of Public Health*.

Memorial to Physician at Queen's University.—Graduates of the Queen's University Faculty of Medicine, Kingston, Ont., have donated a number of old medical books to form the nucleus of a medical history collection to be used as a memorial to Dr. Thomas Gibson, who at the time of his death was professor of the history of medicine at the university.

LATIN AMERICA

Pension Fund for Physicians.—President Batista of Cuba signed a bill on February 20 setting up a pension fund for physicians. The New York *Times* reported that the legislation creates a tax on all pharmaceutical products sold in Cuba and on the fees paid by members of cooperative health associations. Physicians will contribute 3 per cent of their earnings.

FOREIGN

Chadwick Lectures.—The series of Chadwick Public Lectures, arranged by the Chadwick Trust, Abbey House, Westminster, appears in the *British Medical Journal* as follows: M. Greenwood, February 23, on "Social and Industrial Environment and Disease"; Dr. R. Cruickshank, March 16, "Some Postwar Problems in the Control of Infectious Diseases"; Mr. T. Sharp, April 6, "Town Planning and Public Health"; Dr. C. F. White, May 11, "Health Problems in Rebuilt London," and Mr. F. J. Chittenden, June 17, "Plants Causing Irritation."

Government Services

Results of Tuberculosis Surveys

Seventy-seven war industries in eleven different states were surveyed by the eight 35 mm. photofluorographic units operating in industry prior to February 1, according to the Office of Tuberculosis Control of the United States Public Health Service. A total of 194,896 individuals were x-rayed. Tabulations on results of the x-ray examination are available for 125,190 people. Of these, 1,631, or 1.3 per cent, were found to have significant pulmonary tuberculosis. The distribution of the positive cases by stage of the disease was as follows: 874, or 53.6 per cent, minimal; 707, or 43.3 per cent, moderately advanced, and 50, or 3.1 per cent, far advanced. In the District of Columbia 28,098 government workers have been x-rayed. Exactly 300 cases (1.1 per cent) of pulmonary tuberculosis have been discovered. Of these 182 (60.7 per cent) were minimal, 106 (35.3 per cent) moderately advanced and 12 (4.0 per cent) were far advanced. In addition, 1,300 workers at the National Institute of Health have been x-rayed. Among these, 15 cases of tuberculosis were found, 9 minimal and 6 moderately advanced.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 27, 1943.

Reaction of Medical Association to the Beveridge Scheme

In a previous letter to THE JOURNAL (January 9, p. 142) the Beveridge Report, which is a comprehensive scheme of social insurance, with freedom from want as its goal, was described. It is of profound importance to the medical profession, for it proposes that the state should provide medical care, domiciliary as well as hospital, for all. This might mean the extinction, or something near that, of private practice and conversion of the medical profession into state officials. Various committees of the British Medical Association have been studying the report, and their recommendations have been brought before the council, which has framed a motion for transmission to the representative body of the association. This motion recommends that if Parliament accepts the report as a whole, including a scheme for comprehensive health and rehabilitation services for the prevention and cure of disease and restoration of capacity to work, available to all members of the community, the association would be willing to cooperate in the preparation of such a scheme, provided (1) that the character, terms and conditions of the medical service are determined by negotiation and agreement with the medical profession; (2) that the members of the community who decide not to avail themselves in part or in whole of the benefits of the service open to them should not be precluded from obtaining the medical services they desire from doctors within the scheme, paying for such services privately, with the necessary safeguards to prevent abuse. This recommendation will be considered by a special meeting of the representative body and of the panel conference and by a joint meeting of the two at the end of March. In the interval the divisions of the association will consider the council's recommendation.

The decision of the council is evidentiy due to two considerations: The medical profession could not refuse cooperation with the Beveridge scheme of social reform, from which so much is hoped, if it is adopted by Parliament. The majority of the profession is opposed to the total abolition of private practice and the conversion of physicians into government officials. To prevent this, the second provision of the council's recommendation has been framed.

Scheme for the Prophylaxis of Tetanus

The prophylactic scheme against tetanus differs in the British and American armies. The American army, like the Canadian, relies entirely on active immunization, while the British uses also passive immunization. The soldier gets a dose of toxoid on joining, a second dose about six weeks later and a further dose every twelve months. According to the *Army Medical Bulletin* (November 1942) this procedure sets up a "shadow factory" for antitoxin and keeps it in commission but it does not maintain the circulating antitoxin at a constant high level. When tetanus organisms enter the body there may be a danger period of several days before the shadow factory begins to produce antitoxin in quantity, and it is necessary to protect the patient during this danger period by giving him antitoxin, at least 3,000 units as soon as possible after he is wounded. This routine passive immunization has the advantage that it covers any men who may have refused or escaped active immunization. But such men will require two extra doses of 3,000 units at weekly intervals to make them safe.

In the American army active immunization is compulsory and is carried further. Not only does the recruit receive three spaced injections of toxoid but on entering a theater of war he has a fourth dose and renewal doses every four months thereafter. The American authorities believe that these inoculations maintain so high a level of circulating antitoxin that passive immunization after wounding is unnecessary. Instead of antitoxin, American soldiers are given a final "boosting" dose of toxoid.

As in warfare American wounded may be brought to British hospitals and vice versa, the following arrangement has been made: The American authorities have asked that their soldiers should receive a boosting dose of toxoid instead of the British dose of antitoxin, and the Canadian authorities have made the same request. This will be done whenever possible. On the other hand the American authorities have agreed that British wounded in American hospitals shall receive prophylactic antitoxin.

Medical Research in the Army

The medical corps of the British army has a long and distinguished record of medical research. To it is due much of our knowledge of disease in the British colonies. It now has medical research sections at home and abroad, whose task is to bring to light urgent problems and advise on their solution. The *Army Medical Bulletin* for November 1942 points out that the health of a mechanized army is a matter of infinite detail and roving research cannot cover the whole ground. Often the person most likely to know what is needed is the junior medical officer who lives among the troops. He is in the best position to detect avoidable causes of sickness, disability and overstrain.

In industrial medicine the emphasis shifted a few years ago from the cure to the prevention of disease and is now shifting toward the maintenance of health in each particular occupation. The same is happening in the army. It is for the medical officer to notice the cramped position, the visual fatigue, the failure of vitality, the cold hands, the diarrhea or the incipient heat stroke. Medical officers who have noted specific problems of bodily or mental efficiency susceptible of solution by themselves or others are asked to forward them to the Director of Medical Research to the Army, whose task is to coordinate investigations and initiate inquiries.

The role of the medical services as experts in all that concerns the human factor in welfare has been formally recognized by the military authorities. For some time the army council has had a scientific adviser, Sir Charles Darwin, F.R.S., but he and his staff are concerned only with weapons, equipment and ways of making war. A need was felt for a complementary adviser on the biologic side. The director of medical research, Brigadier F. A. E. Crew, F.R.S., will henceforth fulfil this function on the same level as the scientific adviser. In doing so he will require all possible information, on great matters and on small, from the periphery and especially from the field.

Sir William Arbuthnot Lane

Sir William Arbuthnot Lane has died in his eighty-seventh year. He was trained at Guy's Hospital, passing the examination for fellowship of the Royal College of Surgeons when he was only 26. His first appointment was demonstrator of anatomy at Guy's, to be followed by surgeon to the Hospital for Sick Children, Great Ormond Street, and assistant surgeon to Guy's. He published a long series of papers on the most diverse subjects marked by daring originality. His first surgical innovation was excision of a piece of rib in treating an empyema, his next to operate for cleft palate early in life. He introduced the screwing or plating of fractures of long bones when accurate apposition could not otherwise be obtained. He published "The Operative Treatment of Fractures." His skill in the operative

treatment of comminuted fractures of the femur was amazing. He was much interested in the disorders of the skeleton, which he traced to pressure changes induced by the patient's occupation. He pointed out that these changes revealed the work done during life. Thus the skeleton of the cobbler or the washerwoman was characteristic, and the effect of the corset on the abdominal viscera affected the mechanics of the foot. He saw in the skeleton the crystallization of lines of force. He boasted that he could tell in the dissecting room the occupation followed during life by a manual worker. At the beginning of the century he began to teach that much ill health was due to stagnation in the large intestine (intestinal stasis). He denounced the usual view that one daily evacuation was sufficient and said that if man reverted to the habit of three motions daily many diseases, including cancer, would disappear. He described a kink due to formation of thin tags of peritoneum which anchored the iliac colon. These he attributed to excessive straining caused by fecal accumulation in the colon. He treated some cases by excision of the colon. A great fighter, his failure to convince the profession only spurred him to increased polemics in the form of many papers, culminating in his book "The Operative Treatment of Chronic Constipation." He felt so strongly on the subject that he resorted to the lay press and ended by resigning his membership in the British Medical Association and founding the New Health Society to promote his hygienic gospel. Thus a great surgeon ended a long life as a medical crank.

BUENOS AIRES

(From Our Regular Correspondent)

Jan. 12, 1943.

The Faculty of Medicine of Rosario

The Faculty of Medicine of Rosario, founded in 1920, is formed now by the schools of medicine, odontology, pharmacy, biochemistry, obstetrics, legal medicine and pediatrics and is one of the various faculties of the University of the Litoral. The number of students has grown from 173 in 1920 to 3,600 at present. Up to 1940 a total number of about 2,800 professionals, including more than 1,000 physicians, have graduated from the faculty. The development of scientific research work has been hindered to some extent because of the shortage of money and of research material. Only a group of teachers among those who work on a full time program are devoted to both teaching and research. Several medical societies of the various medical specialties have been founded by the members of the various departments of the faculty, scientific journals have been established and a large assembly hall founded. The hospital Nacional Centenario with 650 beds is the main focal point of the faculty. The number of hospitalized and ambulatory patients who have consultation and medical care annually is 10,000 and 100,000 patients respectively. There are also clinics of all the specialties, an institute of psychiatry, a hospital for the insane and a school for children with retarded mentality. There are also a central library of the faculty and a classic library of the chair of history of medicine.

Public Health in Paraguay

General Don Higinio Moringo M., the president of Paraguay, in his presidental message, recently delivered, spoke on the constant progress of the national organization of public health in the country. The problems of hygiene and public health are given proper attention all through the country, even in the remote villages and rural places. An antimalarial crusade was recently successfully completed notwithstanding the fact that malaria had rapidly flared up all through the country in violent form. New hospitals are in construction, and those which are already functioning are modernized. Industrial hygiene is also improved. Laws have been given by which workers and their families have free medical care and drugs. The antituberculosis crusade is directed by a committee of specialized experts. New posts for free distribution of milk for infants and centers for therapy of venereal and syphilitic diseases have been opened to the public. The organization of a national department of nutrition and studies for establishment of obligatory social insurance are in progress.

Malignant Lymphogranulomatosis

Dr. A. A. Ferraris recently reported clinical studies on 15 children who suffered from malignant lymphogranulomatosis in the Hospital of Niños of Córdoba. The patients between the ages of 5 and 12 years were all boys except 1. The disease began with a ganglionic tumor of slow development in the neck in 12 cases. In 3 cases the disease began with acute abdominal symptoms which suggested an emergency operation. There was splenomegaly in 70 per cent of the cases and moderate hepatomegaly in 60 per cent of the cases. The Mantoux intradermal test was carried on in all cases in concentrations of 1:10; positive results were observed in only 2 patients. The same proportion of positivity is obtained in normal children of the city. Two patients had pruritus. Twelve had moderate fever and 3 had no fever. There was a moderate leukocytosis with neutrophilia and without eosinophilia in all cases, notwithstanding that the ganglions showed a large number of polymorphonuclear eosinophils on microscopic study. There was leukopenia with figures varying between 4,000 and 2,000 leukocytes in 3 cases. There were also changes in the erythrocytes of the type of hypochromic anemia. In all cases the histopathologic study of the enlarged ganglions gave results for a proper diagnosis of the disease and the Stenberg cells were found in the specific granulation tissue. The Stenberg cells were scanty in some cases and abundant in some, whereas the polymorphonuclear eosinophils were abundant in all cases. Giant cells similar to those of Langhans were observed in the blood of 2 patients with and without positive results of the Mantoux test respectively. The microsopic study of material obtained during a necropsy showed the ordinary involvement of the various organs by the disease. In the bone marrow of the sternum and of other bones the hemopoietic tissue was replaced by granulation tissue only partially (in foci) and late in course of the disease. In all cases death occurred within one to five years notwithstanding that roentgen therapy was administered.

Erythroblastic Anemia

Dr. M. Acuña, president of the Society of the Instituto de Pediatria y Puericultura of the Hospital de Clínicas of Buenos Aires, in a recent lecture before this society said that erythroblastic anemia of Cooley's type in infants (also called erythroblastic anemia of either von Jaksch's or Luzet's type) should be differentiated by any of these names from any other forms of anemia in infants. The speaker reported two series, one of 4 and another of 7 cases. The clinical course consisted in early appearance of progressive anemia, hepatomegaly, splenomegaly, presence of erythroblasts in the blood, osteoporosis of the skeletal bones, congenital familial ethnic character and lack of any disease which could have been considered as cause of anemia. All the patients formerly lived in the Mediterrean area. There were several patients in the family of all patients but there were also normal children. Even in couples of twins one was ill and the other was normal. The disease appeared in the course of the first six months of life of the patients and was of the typical form when the infants reached 1 year of age. The cause was unknown in all cases. The 4 patients in the first series and 6 patients of the second series died. The patient in the second group who is still living is in a grave condition.

Deaths

Arnold Carl Klebs, Nyon, Switzerland, medical humanist and student of the scientific and medical literature of the 15th century, died at his villa Les Terrasses, Nyon, March 6, aged 72.

Dr. Klebs was born in Berne, Switzerland, March 17, 1870. He was a son of Dr. Edwin Klebs who, with Loeffler, had discovered the diphtheria bacillus. After his graduation in 1895 at the Universität Basel Medizinische Fakultät, Dr. Klebs was for a time assistant in the polyclinic at the Basel University and pathologic instructor at the University of Zurich. In 1896 he came to the United States and devoted himself to the study of tuberculosis. For a time he was head of the tuberculosis sanatorium at Citronelle, Ala., later going to Chicago, where his father had been professor of pathology at Rush Medical College since 1896. In 1904 he became a citizen of the United States. During his years in Chicago he served as consulting physician to the Cook County Institutions and as director of the Chicago Tuberculosis Institute. Dr. Klebs returned to Switzerland in 1909; from 1915 to 1918, Washington, D. C., and 1918 to 1919, New York, where he returned again for one year in 1926. Dr. Klebs was vice president of the section on preventive diseases of the International Congress on Hygiene, Washington, in 1912. At one time he had held membership in the American Clinical and Climatological Association, the National Tuberculosis Association and numerous foreign and scientific societies. When Dr. Klebs took up permanent residence in Switzerland he dropped his membership in the Illinois State Medical Society and fellowship in the American Medical Association.

Following the last war Dr. Klebs came to the United States once each year until 1930, when poor health forced him to abandon his annual expeditions. His last trip was in April 1939, when he came secretly to surprise the late Dr. Harvey Cushing on his seventieth birthday, which the Harvey Cushing Society was celebrating in New Haven, Conn.

Dr. Klebs had written extensively on medical and historical subjects. In 1909 he was the editor of the American Treatise on Tuberculosis; History of Variolation, 1914; Leonardo da Vinci Studies, 1916; Tuberculosis and Military Organization, 1917; Bibliography of Medical Incunabula, 1917, 1918; Early Herbals (Lugano), 1925, and Incunabula Scientifica et Medica, 1938. Dr. Klebs was a close friend of Osler, Welch and Cushing and it was because of his long friendship with Cushing that he became affiliated with Yale and the Yale Medical Library.

William Hoffman Gardner Logan ✠ Chicago; Chicago College of Dental Surgery, 1896; American College of Medicine and Surgery, Medical Department of Valparaiso University, 1903; dean of the faculty and professor of plastic and oral surgery at the Chicago College of Dental Surgery Dental School of Loyola University; past president of the National Dental Association, Illinois State Dental Society, Chicago Dental Society, the seventh International Dental Congress and the American Association of Dental Schools; formerly vice president and president of the International Dental Federation; specialist certified by the American Board of Plastic Surgery; member of the American Association of Oral and Plastic Surgeons; fellow and a member of the board of governors of the American College of Surgeons; during World War I served as chief of the dental division of the Surgeon General's Office in Washington, D. C.; member of the general medical board of the Council of National Defense; secretary from 1929 to 1933 and member of the board of governors from 1933 to 1941 of the Gorgas Memorial Institute of Tropical and Preventive Medicine; received the honorary degrees of doctor of laws from Loyola University in 1926 and the National University of Ireland, Dublin, in 1940; master of science from the University of Michigan, Ann Arbor, in 1930; was awarded the William Jarvie Fellowship Medal of the Dental Society of the State of New York; senior attending surgeon in oral surgery at the Michael Reese Hospital; on the staffs of the Cook County and St. Joseph's hospitals; aged 70; died, April 6, of coronary thrombosis.

James Bassett McElroy ✠ Memphis, Tenn.; College of Physicians and Surgeons, Baltimore, 1893; professor of medicine, for many years chief of the division of medicine and at one time acting dean, member of the board of trustees and chairman of the faculty of the University of Tennessee College of Medicine; formerly professor of pathology at the Memphis Hospital Medical College, where in 1905 he served as chief of the dispensary and as lecturer in physical diagnosis; specialist certified by the American Board of Internal Medicine; secretary of the Section on Practice of Medicine of the American Medical Association, 1902-1903; past president of the Tennessee State Medical Association and the Memphis and Shelby County Medical Society; member of the Southern Medical Association and the American Society of Tropical Medicine; fellow and ex-governor of the American College of Physicians; chief of staff and physician in chief of the medical division of the Memphis General Hospital, now known as the John Gaston Hospital; on the staff of the Baptist Memorial Hospital; in 1934, at the commencement exercises of the University of Tennessee College of Medicine, his portrait was presented to the university by members of the faculty and the alumni; aged 76; died, March 24.

William Birket Arnold, St. Albans, Vt.; Bellevue Hospital Medical College, New York, 1888; member of the Vermont State Medical Society; served as city health officer and city physician for many years; on the staff of St. Albans Hospital; aged 83; died, February 27, of heart disease.

Walter Milo Barnum, Kent, Conn.; College of Physicians and Surgeons, New York, 1883; also a druggist; aged 83; died, February 19, of coronary occlusion.

Robert Lee Beaumont, Kansas City, Mo.; Beaumont Hospital Medical College, St. Louis, 1889; aged 80; died, January 20, in the Armour Memorial Home of chronic myocarditis.

Sylvester Robert Best, Gary, Ind.; Ohio Medical University, Columbus, 1898; member of the Indiana State Medical Association; aged 70; died, February 13, in St. Mary's Mercy Hospital of coronary occlusion.

James Emmett Blagg, Philadelphia; Eclectic Medical Institute, Cincinnati, 1905; member of the Medical Society of the State of Pennsylvania; aged 67; died recently in the Jewish Hospital of coronary thrombosis.

John Willet Bruner ✠ Bloomsburg, Pa.; Jefferson Medical College of Philadelphia, 1890; fellow of the American College of Surgeons; aged 77; instrumental in the founding, surgeon in chief on the staff and member of the board of directors of the Bloomsburg Hospital, where he died, February 10, of uremia.

Cornelius E. Cain, Whitley City, Ky.; Barnes Medical College, St. Louis, 1901; a director of the Bank of McCreary County; aged 70; died, February 6, in Washington, D. C., of brain tumor.

Hanford Carvell, Gloucester, Mass.; Baltimore Medical College, 1910; member of the Massachusetts Medical Society; aged 67; member of the senior staff of the Addison Gilbert Hospital, where he died, February 15, of virus pneumonia and myocarditis.

William Cogswell Clarke, Cornwall Bridge, Conn.; Columbia University College of Physicians and Surgeons, New York, 1899; member of the Connecticut State Medical Society; served as professor of experimental surgery at his alma mater and surgical pathologist to the Presbyterian Hospital, New York; member of the consulting staff of the Sharon (Conn.) Hospital; aged 71; died suddenly, February 14, of coronary occlusion.

William Henry Conner, Fort Wayne, Ind.; Howard University College of Medicine, Washington, D. C., 1894; aged 81; died, February 19, of influenza and myocarditis.

Augustus Ernest Cordes ✠ Brooklyn; Albany (N. Y.) Medical College, 1899; served during World War I; aged 70; died, February 14, of coronary thrombosis.

Edward F. W. Crawford, La Porte, Ind.; Detroit College of Medicine, 1894; member of the Indiana State Medical Association; aged 73; on the staff of the Holy Family Hospital, where he died, February 4, of myocarditis.

Oren Louis Cuddy, Lincoln, Mo.; Barnes Medical College, St. Louis, 1903; member of the Missouri State Medical Association; past president of the Benton County Medical Society; for thirty years local and dispensing surgeon for the Missouri Pacific Railway Company; for ten years served as city physician; served on the advisory board and as a member of the medical reserve corps during World War I; aged 67; on the staff of the Bothwell Memorial Hospital, Sedalia, where he died, February 19, of pneumonia and coronary embolism.

Charles Louis Davis, Batavia, N. Y.; University of Buffalo School of Medicine, 1907; member of the Medical Society of the State of New York; served on the staffs of the Batavia and St. Jerome hospitals, New York State School for the Blind and the Genesee County Home-Infirmary; aged 60; died, February 19, of carcinoma of the rectum.

Francis Asbury De Mand ✠ Oklahoma City; University of Oklahoma School of Medicine, Oklahoma City, 1917; served in France during World War I; associate in obstetrics at his alma mater; aged 50; on the staffs of St. Anthony Hospital and the University Hospital, where he died, February 11, of rheumatic heart disease.

Albert Edward Doe, Chicago; Chicago Medical School, 1921; a member of the medical department of the Chicago Rapid Transit Company; aged 61; died, February 13, in the Albert Merritt Billings Hospital of pneumonia following an operation.

Joseph Alexander Driscoll, Brooklyn; Long Island College Hospital, Brooklyn, 1908; formerly physician to the District Attorney's office; served on the staffs of St. Catherine's and the Caledonian hospitals; aged 56; died, February 18, of cerebral hemorrhage and uremia.

Joseph Baylis Earle, Greenville, S. C.; University of Virginia Department of Medicine, Charlottesville, 1886; member of the South Carolina Medical Association; formerly medical director of the Pioneer Life Insurance Company and the Liberty Life Insurance Company; aged 80; died, February 10, of heart disease.

Lewis H. Edwards, Monroeville, Ind.; Fort Wayne College of Medicine, 1883; aged 82; died, February 12, in the Adams County Memorial Hospital, Decatur, of chronic myocarditis and pneumonia.

Adolf A. Eisenheimer, Akron, Ohio; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1912; aged 56; died, February 15, of coronary occlusion.

Jacob Nathaniel Feinberg ✠ Long Island City, N. Y.; University and Bellevue Hospital Medical College, New York, 1914; on the staff of St. John's Long Island City Hospital; vice president and on the staff of the Boulevard Hospital, where he died, February 10, of coronary thrombosis, aged 53.

Attilio H. Giannini, Los Angeles; University of California Medical Department, San Francisco, 1896; for many years a banker and motion picture executive; aged 68; died, February 7, of heart disease while attending a meeting of the board of trustees of Loyola University.

Earl P. Gray, Wilkinsburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1897; aged 73; died, February 24, of chronic nephritis and cirrhosis of the liver.

Lesser Bernhardt Groeschel ✠ Mount Vernon, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1906; specialist certified by the American Board of Radiology, Inc.; member of the American Roentgen Ray Society and the American College of Radiology; roentgenologist at the Northern Westchester Hospital, Mount Kisco, St. Joseph's and the Professional hospitals, Yonkers, and the Seton Hospital, New York; aged 56; died, February 23, in Scarsdale of coronary thrombosis.

Elmer Garrison Harris, Los Angeles; National University of Arts and Sciences Medical Department, St. Louis, 1918; served in the medical corps of the U. S. Army during World War I; on the staff of the Presbyterian Hospital-Olmsted Memorial; aged 50; died, February 14, in the Veterans Administration Facility, West Los Angeles, of spinal sclerosis.

George Frey Hermann Sr., Cincinnati; Cincinnati College of Medicine and Surgery, 1896; aged 72; died, February 20, in the Bethesda Hospital of coronary disease.

Charles Clinton Hoagland, Berkeley, Calif.; Northwestern University Medical School, Chicago, 1906; served on the staff of the Ernest V. Cowell Memorial Hospital, University of California; aged 63; died, February 10, of coronary occlusion.

Alvah Alexander Howell, New Lebanon, Ohio; Starling-Ohio Medical College, Columbus, 1911; aged 65; died, February 15, in the Miami Valley Hospital, Dayton, of pulmonary tuberculosis.

John Preston Huff, Carterville, Ill.; St. Louis College of Physicians and Surgeons, 1909; aged 62; died, February 25, of cerebral hemorrhage.

Sergius M. Ingerman, New York; Universität Bern Medizinische Fakultat, Switzerland, 1889; member of the Medical Society of the State of New York and the American Academy of Ophthalmology and Otolaryngology; past president of the Russian Medical Society; aged 74; consultant in ophthalmology at the Beth David Hospital, where he died, February 18, of cerebral hemorrhage.

George Boerstler Kistler, Newcomerstown, Ohio; Columbus Medical College, 1892; member of the Ohio State Medical Association; past president of the Tuscarawas County Medical Society; aged 76; was found dead in bed, February 15.

Albert Joseph Lawler ✠ Niagara Falls, N. Y.; Niagara University Medical Department, Buffalo, 1898; fellow of the American College of Surgeons; on the staff of St. Mary's Hospital; aged 65; died, February 16, of burns received when his clothes ignited while he was smoking.

James M. Lemons, Pine Bluff, Ark.; Memphis (Tenn.) Hospital Medical College, 1893; member and past president of the Arkansas Medical Society and the Jefferson County Medical Society; aged 80; died, February 3, of arteriosclerosis and chronic nephritis.

Clarence M. Lentz, Albemarle, N. C.; North Carolina Medical College, Charlotte, 1909; past president and secretary of the Stanly County Medical Society; served as county coroner; on the staff of the Yadkin Hospital; aged 57; died, February 13, of coronary thrombosis.

Edgar Miller Long, Hamilton, N. C.; University of Maryland School of Medicine, Baltimore, 1909; aged 56; died, February 24, in the Park View Hospital, Rocky Mount, of adrenal insufficiency.

Emil Lustig, St. Petersburg, Fla.; University of the City of New York Medical Department, 1883; member of the Florida Medical Association; also a pharmacist; medical examiner for the Selective Service Board in Buffalo during World War I; served on the staff of the Mound Park Hospital; aged 86; died, February 23, of heart disease.

George Lyford, Cincinnati; University of Cincinnati College of Medicine, 1925; member of the Ohio State Medical Association; on the staffs of the Cincinnati General and the Christian R. Holmes hospitals; medical director of the Union Bethel Clinic; aged 44; died, February 15, in the Christ Hospital of pneumonia and myocarditis.

John Current McIntire, St. Louis; University of Louisville (Ky.) Medical Department, 1898; member of the Missouri State Medical Association; aged 66; on the staff of the Christian Hospital, where he died, February 16, of myocarditis.

Sterling Price Martin, Blytheville, Ark.; Barnes Medical College, St. Louis, 1903; served as city health officer; aged 70; died, February 1, in the Walls Hospital of angina pectoris.

Americus Vespucius Menefee, Covington, Ky.; Louisville (Ky.) Medical College, 1892; member of the Kentucky State Medical Association; served during World War I; aged 71; on the staff of St. Elizabeth Hospital, where he died, February 17, of lobar pneumonia.

Henry Taylor Miller ✠ Washington, D. C.; University College of Medicine, Richmond, Va., 1905; aged 61; staff surgeon at the Episcopal Eye, Ear and Throat Hospital and the Doctors Hospital, where he died, February 7, following an operation for prostatic hypertrophy, paralytic ileus and heart disease.

Alney Neal Minear, Inglewood, Calif.; Medico-Chirurgical College of Kansas City, Mo., 1905; member of the Utah State Medical Association; for many years practiced in Salt Lake City; aged 74; died, January 11, in a hospital at Los Angeles of nephritis.

Brutus Caesar Moore, Albemarle, N. C.; Jefferson Medical College of Philadelphia, 1886; aged 86; died, February 22, of coronary thrombosis.

Julia Mary Lombard Moriarty, Newton, Mass.; Boston University School of Medicine, 1895; aged 70; died, February 16, in the Massachusetts General Hospital, Baker Memorial, Boston, of hemorrhage and duodenal ulcer.

Ralph Luther Morse ✠ Norwalk, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; on the staff of the Norwalk Memorial Hospital; aged 68; died, February 21, of influenza and heart disease.

Charles Borromeo O'Rourke, East Providence, R. I.; Baltimore Medical College, 1907; member of the Rhode Island Medical Society; served during World War I; medical examiner for East Providence for many years; head of the medical examining board of the local draft board; on the staff of St. Joseph's Hospital; formerly chairman of the East Providence branch of the Providence Chapter of the American Red Cross; aged 58; died, February 13, in Providence of acute myocarditis.

Milton Jay Parke, Lakewood, Ohio; Western Reserve University Medical Department, Cleveland, 1890; formerly on the staffs of St. John's and St. Vincent Charity hospitals, Cleveland; aged 79; died, February 9, of coronary sclerosis.

James Fred Pfahler, Berwick, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; member of the Medical Society of the State of Pennsylvania; served on the Berwick Hospital; on the board of health and school board; aged 65; died suddenly, February 8, of coronary thrombosis.

Don Pierce, Wyaconda, Mo.; Barnes Medical College, St. Louis, 1901; member of the Missouri State Medical Association; aged 68; died recently of pneumonia and arthritis.

John Hunter Pope, Tyler, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1918; served during World War I; member of the staff of the Mother Frances Hospital; aged 48; died, February 12, of a gunshot wound received while he was cleaning a pistol.

Katherine Porter, Palo Alto, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1898; aged 72; died recently of cerebral hemorrhage.

George William Purefoy, Asheville, N. C.; Jefferson Medical College of Philadelphia, 1876; at one time a member of the county board of health; formerly on the staff of the Asheville-Biltmore Sanitarium, Biltmore; aged 92; died, February 23, of arteriosclerosis.

Paul Emil Rauschenbach, Paterson, N. J.; University of Virginia Department of Medicine, Charlottesville, 1904; member of the Medical Society of New Jersey; formerly served as city physician; aged 70; for many years served as director of the orthopedic clinic at the Paterson General Hospital, where he died, February 23, of embolism, heart disease and pneumonia.

James Denny Reed, Covina, Calif.; Bellevue Hospital Medical College, New York, 1883; formerly served on the school board, as president of the Chamber of Commerce and as bank president; aged 84; died, January 29, in the Covina Hospital of pneumonia.

Francis Gurney Reese ✠ Coudersport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; served as president of the Potter County Medical Society and also as a member of its board of censors; formerly health officer; aged 72; died recently of carcinoma of the pancreas.

John Franklin Reynolds, Mount Sterling, Ky.; Hospital College of Medicine, Louisville, 1890; died, February 10, of myocarditis, arteriosclerosis and gangrene of the right foot.

William Bernard Riley, Lawrence, Mass.; Harvard Medical School, Boston, 1911; served as city bacteriologist, examiner for the Selective Service Board number 80 and examiner for the federal industrial accident board; aged 58; died, February 12, in the Lawrence General Hospital of cerebral hemorrhage.

Francis Emerson Rosenberger ✠ Oklahoma City; Beaumont Hospital Medical College, St. Louis, 1901; member of the Oklahoma County Sanity Board; served on the medical advisory board during World War I; aged 68; died, February 8, in the Polyclinic Hospital of heart disease.

Jacob Coby Rosenblueth, New York; College of Physicians and Surgeons, New York, 1892; member of the Medical Society of the State of New York; aged 71; died, February 21, of carcinoma.

Abram S. Samuels ✠ Baltimore; College of Physicians and Surgeons, Baltimore, 1898; also a pharmacist; clinical professor of gynecology at the University of Maryland School of Medicine and College of Physicians and Surgeons; member of the Society of American Bacteriologists; fellow of the American College of Surgeons; served on the staffs of the Mercy and Sinai hospitals; aged 66; died, February 7, of coronary thrombosis.

Howard William Schaffer ✠ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1921; diplomate of the National Board of Medical Examiners; aged 46; on the staffs of the Memorial Hospital, Germantown Hospital and the Philadelphia General Hospital, where he died, February 11, of carcinoma of the bladder.

Walter Jordan Sener, Media, Pa.; Temple University School of Medicine, Philadelphia, 1911; member of the Medical Society of the State of Pennsylvania and of the American Academy of Ophthalmology and Otolaryngology; aged 66; died recently of coronary occlusion.

Harriet Belle Henry Short, Riverside, Calif.; Northwestern University Woman's Medical School, Chicago, 1899; aged 71; died, January 31, of myocarditis.

Percy Clinton Snowden, Peekskill, N. Y.; University of Vermont College of Medicine, Burlington, 1893; member of the Medical Society of the State of New York; formerly on the staff of the Peekskill Hospital; aged 74; died, February 7, in the University Hospital, Coral Gables, Fla., of pneumonia.

George Omar Speirs ✠ Spearville, Kan.; Rush Medical College, Chicago, 1900; fellow of the American College of Surgeons; formerly secretary of the Ford County Medical Society; councilor of the Twelfth District of the State Medical Society; formerly mayor of Ellinwood; served on the city council and as mayor of Spearville for several terms; recently an examiner for the Hodgeman County draft board; on the staffs of St. Anthony's Hospital, Dodge City, and the Perkins Hospital; aged 67; died, January 28.

James Wesley Stack, Crumpton, Md.; University of Maryland School of Medicine, Baltimore, 1893; past president of the Queen Annes County Medical Society; served as magistrate at Crumpton for many years; judge of the Queen Annes County Orphans' Court from 1934 to 1938; aged 75; died, January 31.

Joseph Francis Xavier Stack, Hoboken, N. J.; Bellevue Hospital Medical College, New York, 1896; health commissioner of Hoboken for thirty-three years; aged 71; on the staff of St. Mary's Hospital, where he died, February 17, of bronchopneumonia and cerebral hemorrhage.

Earl Minor Stewart, Eagle, Neb.; College of Physicians and Surgeons, Baltimore, 1900; at one time practiced in Imperial, where he had for sixteen years been a member of the Chase County High School Board, a county coroner, vice president of the Farmers and Merchants Bank and chairman of the Chase County Red Cross; aged 71; died, February 14, in Lincoln of terminal hypostasis due to cerebral arteriosclerosis.

Edward von Toll, Pasadena, Calif.; St. Louis College of Physicians and Surgeons, 1905; aged 75; died recently of hypostatic pneumonia.

Otto Theodore Walser, St. Louis; Marion-Sims-Beaumont Medical College, St. Louis, 1902; aged 62; served on the staff of the Evangelical Deaconess Home and Hospital, where he died, February 4, of heart disease.

Edward Spann Warlick, Asheville, N. C.; University of Nashville (Tenn.) Medical Department, 1888; also a druggist; aged 76; died, February 5, in the Aston Park Hospital of heart disease.

John Thomas Welch, Chicago; Chicago Homeopathic Medical College, 1901; aged 77; died, February 6, of carcinoma of the colon.

Walter Balthasar Wellbrock, Lindenhurst, N. Y.; Long Island College Hospital, Brooklyn, 1901; at one time village trustee, school physician and mayor of Lindenhurst; visiting physician to Dr. King's Hospital, Bay Shore; aged 67; died, February 3, of coronary thrombosis.

William Willing Wilkinson ✠ Phoenix, Ariz.; Northwestern University Medical School, Chicago, 1901; member of the staff of St. Joseph's Hospital and the Good Samaritan Hospital; aged 73; died, January 27, of injuries received when his automobile was struck by a train.

Samuel William Woodhouse Jr., Philadelphia; Jefferson Medical College of Philadelphia, 1895; formerly curator and acting director of the Philadelphia Museum of Art; medical director of the American Red Cross in southern France during World War I; aged 69; died, February 1, of cerebral hemorrhage.

DIED WHILE IN MILITARY SERVICE

Thomas Henry Cheavens ✠ Dallas, Texas; Baylor University College of Medicine, Dallas, 1928; since 1938 associate professor of clinical neuropsychiatry at his alma mater, where he was assistant in clinical neuropsychiatry from 1929 to 1931, instructor from 1931 to 1935 and assistant professor from 1935 to 1938; member of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology, Inc.; dispensary neuropsychiatrist and associate neuropsychiatrist, Baylor and Parkland hospitals; on the staff of the Timberlawn Sanitarium; began active duty in April 1942 as a lieutenant commander in the medical corps of the U. S. Naval Reserve; psychiatrist at the U. S. Naval Hospital, San Diego, Calif., where he died, February 23, of hemorrhagic encephalitis, aged 39.

John Thompson Shaffer ✠ Sellersville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1929; served as president of the Bucks County Medical Society; on the staff of the Grand View Hospital; an examining physician for the Bucks County Draft Board number 4 at Quakertown; extended active duty began in May 1942 as a captain in the medical corps, Army of the United States, attached to the 321st Air Base Squadron, Kellogg Field, Battle Creek, Mich., where he died, February 21, of coronary occlusion, aged 38.

Correspondence

PHYSICIANS MUST VOLUNTEER FROM LARGE CITIES

To the Editor:—The editorial entitled "Physicians Must Volunteer from Large Cities" in the March 27 issue of The Journal states that "the responsibility" for the lagging in procurement of medical officers "rests unquestionably on the failure of young available physicians in the large cities of the country, particularly those of the eastern seaboard, to volunteer," and for a solution recommends "the pressure of public opinion."

But why are available physicians from the cities not volunteering? These men are no less patriotic than their country cousins and are just as eager to do their part. They resent, however, the fact that many physicians within the draft age are considered "essential" for hospital work, part time teaching, part time research or part time industrial work, an arrangement which permits these men to continue their private practice. The others feel that their obligations and family responsibilities are as great as those of the "essential" men in their own age group. They are particularly disturbed about single men in this deferred category. They know that there are enough qualified men over draft age in cities to take over all part time hospital and clinical work. They feel that whatever medical research is necessary to the war effort should be done on a full time basis, preferably under the direct supervision of the Army and Navy.

The removal of preferential ratings for part time clinical work or teaching would place all physicians within the draft age on an equal footing. They would then have neither reason nor excuse for not volunteering, and it might be unnecessary to call them "before the bar of public opinion" by publishing their names in medical journals.

Editorial Board, *Norfolk Medical News.*

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OCHRONOSIS

To the Editor:—In The Journal, March 6, page 784, a reference appearing in my abbreviated paper (Ochronosis of the Sclera and Cornea Complicating Alkaptonuria, The Journal, Dec. 19, 1942) is questioned concerning the first British case of ochronosis. Your correspondent infers incorrectly from Dr. F. M. Pope's article (A Case of Ochronosis with a Note on the Relationship of Alkaptonuria by A. E. Garrod, *Lancet* **1**:24, 1906) that "the 11 previously reported (British) cases are mentioned and exact references are listed." The previously reported cases (10) were collected from other countries and can be found in my complete paper appearing in the 1942 Transactions of the Section on Ophthalmology of the American Medical Association. Dr. Pope states (p. 26) "This case is the eleventh reported of this disease and the first from the British Islands. I present in tabular form short abstracts of all the former cases." Only 9 more English cases of ochronosis could be found in my review of the literature. I still believe Cushing's finding that the first British case of ochronosis had been diagnosed as Addison's disease until examined by Osler is worth recording.

James W. Smith, M.D., New York.

PORTAL CIRRHOSIS

To the Editor:—In the March 6 issue of The Journal, page 719, in an article by Carl H. Greene entitled "Physiologic Considerations in the Treatment of Portal Cirrhosis," the statement is made that "the patient with cirrhosis frequently shows a reduction in the prothrombin time of the blood which, if pronounced, will cause a tendency to hemorrhage."

It seems apparent that the author meant to express himself in terms of a reduction of the prothrombin level rather than in terms of a reduction of the prothrombin time. It is the reduction of the prothrombin level of the blood which will cause a tendency to hemorrhage. Such a condition, however, is associated with a prolongation of the prothrombin time and not with a reduction of the prothrombin time as mentioned in the author's paper.

Such terminology may seem confusing to the casual reader. For the sake of clarity it should be emphasized that a reduction of the prothrombin level of the blood (hypoprothrombinemia) is synonymous with a prolongation of the prothrombin time causing the well known tendency to hemorrhage. On the other hand, the increase in the prothrombin level of the blood (hyperprothrombinemia) is associated with a reduction of the prothrombin time, causing a tendency to clot formation.

William Saphir, Captain, M. C., A. U. S.

DANGERS OF TALCUM IN THE PERITONEAL CAVITY

To the Editor:—For the past decade or more, evidence has been accumulating of the occurrence of so-called intraperitoneal granulomas following the accidental implantation of talcum during laparotomy. The talc is shed from the surface of rubber gloves or from collections of the talc powder, which so frequently settles in the tip of the glove fingers and spills therefrom through accidental rips and tears.

Talcum is predominantly a silicate of magnesium and sets up a vicious reactionary adhesive peritonitis, provocative of postoperative intestinal obstruction. I never realized fully the tragic significance of this complication until I encountered it in the postoperative course of my own son.

No one has ever done more than to point out the dangers inherent in talc and to suggest careful depowdering of the surface of the gloves before operating. Consequently we set about to sidetrack the talc evil. After I had made numerous preliminary experiments, Dr. D. J. Verda and Dr. Frank H. Kidd Jr., respectively fellow in surgery and surgical resident in the Barnard Free Skin and Cancer Hospital, interested themselves in the work and have done all of the later experimentation.

This experimentation, although it is not completed in every detail, has now reached the point where we may state with assurance that ordinary cornstarch from every point of view serves as an ideal dusting powder for gloves, causes no undesirable after-effects and is sterilized by ordinary autoclaving.

We are anxious to publish this information in advance of the completion of all our work, so that the basic fact may be available to our armed forces at the earliest possible moment.

M. G. Seelig, M.D., St. Louis.
Director of Pathology, Barnard Free Skin and Cancer Hospital.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospital Service Plans as Insurance.—The plaintiff, a nonprofit hospital service plan corporation organized and operated under the appropriate Ohio law relating to such organizations and licensed to do business by the superintendent of insurance of Ohio, sought to enjoin the state treasurer from collecting from it a franchise tax, which a state statute required the treasurer to collect from corporations engaged in the business of insurance. From a decree in favor of the hospital service plan corporation, the treasurer appealed to the court of appeals of Ohio, Franklin County.

The plaintiff corporation agreed to act as the agent of eighteen charitable hospitals in Cleveland in the sale to the public of a contract which required the subscriber to pay a stated sum periodically to the plaintiff and entitled him in return to hospitalization for a stated period, if deemed necessary by the subscriber's attending physician, in any of the eighteen hospitals that the subscriber might choose. The plaintiff was to pay the hospital selected by the subscriber designated sums according to the type and length of service rendered to the subscriber. Any surplus remaining in the plaintiff's funds, after paying hospital bills and the cost of administration, is held as a reserve for the benefit of the subscribers. This arrangement, the treasurer argued, substantially amounted to insurance and in writing such a contract the hospital service plan corporation was writing a contract of insurance and hence was liable for the franchise tax in question. In support of this contention, the treasurer relied on the definition of "insurance company," set out in the insurance code of Ohio, reading, in part, as follows:

> The term 'insurance company' as used in this chapter includes every corporation, association and society engaged in the business of insurance of any character whatsoever, or engaged in the business of entering into contracts substantially amounting to insurance of any character, or of indemnifying or guaranteeing against loss or damage or acting as surety on bonds or undertakings.

The treasurer also relied on *State ex rel. Duffy* v. *Western Auto Supply Company*, 134 Ohio St. 163, 16 N. E. (2d) 256, an Ohio decision, the second paragraph of the syllabus of which reads as follows:

> Insurance, as related to property and liability, is a contract by which one party promises, upon a consideration, to compensate or reimburse the other if he shall suffer loss from a specified cause, or to guarantee or indemnify or secure him against loss from that cause.

The hospital service plan association argued that the contract it issued assures the subscriber service and not indemnity; that it is essential to a true insurance contract that it provide for payment of money to the insured in an amount, defined in the contract, designed to indemnify him for a loss he has suffered. In our judgment, said the appellate court, the contention of the plaintiff that a contract is not one substantially amounting to insurance unless it provides for the payment of money to the subscriber on the happening of a contingency cannot be adopted. Further, the fact that payment under the contract here in question is made to the hospital and not to the subscriber will not prevent the contract from being a contract of insurance. The advantage to the subscriber, if he invokes the benefits of his contract, requires payment in money which is definitely measured by the extent of service rendered to him by the hospital to which he elects to go. It is payable on a contingency, namely, that it is certified by his attending physician that the subscriber requires hospitalization. The minimum payment is not fixed but the maximum payment that may be exacted from the hospital service plan corporation is set forth in the contract. The contract, in probability, is not to indemnify the subscriber because the hospital which he selects does not extend credit to him and, therefore, there is no primary liability on his part which would be essential to make the hospital service plan corporation an indemnifier. The amount which is paid by the subscriber is a charge based on an actuarial determination of the probable risk incurred in issuing the contract. Although that which is provided the subscriber on the happening of a contingency is, so far as he is concerned, service, yet it is measured by a money consideration payable to the hospital because of the rendering of that service to the subscriber on behalf of the hospital service plan corporation. The language of the section of the insurance code quoted above, in effect, defining a company issuing contract substantially amounting to insurance of any character as an insurance company, is so broad as to require this court to hold that the hospital service plan corporation is an insurance company. The contract in this case in so many particulars amounts substantially to insurance to the subscriber as to require that it be construed to be an insurance contract.

The hospital service plan corporation contended that, even if it was assumed that it was engaged in an insurance business, nevertheless, it was exempt from the payment of the franchise tax imposed on corporations engaged in an insurance business because of a section in the hospital service plan corporation act of Ohio that provides:

> Every corporation subject to the provisions of this act is hereby declared to be a charitable and benevolent institution, and its funds and property shall be exempt from taxation.

Obviously, said the court, the purposes of the plaintiff and the conduct of its business bring it clearly not only within the letter of the act but also within the spirit. In every sense of the term it is a charitable and benevolent institution. The treasurer argued, however, that the franchise tax he sought to collect is not levied on the funds or the property of a corporation but is a tax on the right to carry on the nonprofit hospital service plan and that the exemption accorded the plaintiff corporation from all other provisions of the insurance laws, which is granted by the hospital service plan corporation law of the state, does not preclude liability on the part of the hospital service plan corporation for the franchise tax. Charitable hospitals, answered the appellate court, are exempted from all forms of taxation. The hospital service plan corporation here involved acts as an agent for charitable hospitals. The purpose of the subscription contract the plaintiff corporation offers is twofold: first, to make possible necessary hospitalization for a large part of the public at a low cost, and second, to assure in the aggregate the payment of the hospitals of a larger sum for these services than would otherwise be received and thus to enable the hospitals to render a better and more extended general service. The hospital service plan corporation act exacts the payment from each such corporation licensed to do business in the state of a fee of $250 on the filing of an application for certificate of authority and an annual license fee equal to one tenth of one cent for each contract issued by such corporations and then outstanding. The $250 payment, in itself, is a form of franchise tax and is a prerequisite to the issuance of a certificate which authorizes the hospital service plan corporation to carry on its business. While it is true that it is generally held that a franchise tax is not a tax on property, it should be noted that the language exempting hospital service plan corporations from taxation includes not only property but its funds as well. In view of all of the germane acts, namely, the insurance laws, the taxation statutes and the act relating to hospital service plan corporations, it would seem that it was the legislative intent in enacting the hospital service plan corporation law to exempt such corporations from any liability for taxes of any kind or character or the payment of any sum for the privilege of operating. The legislature as a basis for the granting of certain rights and privileges accorded to nonprofit hospital service plan corporations classified them as benevolent and charitable institutions and set up a comprehensive act under which they were authorized to conduct their business and provided a fee which it deemed adequate in view of the fact that it further provided expressly that the funds and property of such corporation shall be exempt from taxation. This exemption, the court concluded, was intended to be all inclusive.

For the reasons stated, the decree restraining the state treasurer from collecting a franchise tax on the hospital service plan corporation was affirmed.—*Cleveland Hospital Service Association v. Ebright, Treasurer of State, 45 N. E. (2d) 157 (Ohio, 1942).*

Society Proceedings

COMING MEETINGS

HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION, CHICAGO, BEGINNING JUNE 7. DR. OLIN WEST, 535 NORTH DEARBORN ST., CHICAGO, SECRETARY.

Alabama, Medical Association of the State of, Birmingham, April 20-22. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Association of Genito-Urinary Surgeons, Stockbridge, Mass., June 10-12. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.

American Association of Industrial Physicians and Surgeons, Rochester, N. Y., May 25-27. Dr. E. C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association on Mental Deficiency, New York, May 12-15. Dr. Neil A. Dayton, Mansfield Training School, Mansfield Depot, Conn.

American College of Radiology, Chicago, June 6. Mr. Mac F. Cahal, 540 North Michigan Blvd., Chicago, Executive Secretary.

American Gynecological Society, Hershey, Pa., May 31-June 2. Dr. Howard C. Taylor Jr., 842 Park Ave., New York, Secretary.

American Neurological Association, New York, May 6-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., May 31-June 3. Dr. Walter S. Atkinson 129 Clinton St., Watertown, N. Y., Secretary.

American Psychiatric Association, Detroit, May 10-13. Dr. Winfred Overholser, St. Elizabeth's Hospital, Washington, D. C., Secretary.

American Psychoanalytic Association, Detroit, May 9-11. Dr. Leo H. Bartemeier, General Motors Bldg., Detroit, Secretary.

American Society of Clinical Pathologists, Chicago, June 4-6. Dr. Alfred S. Giordano, 531 North Main St., South Bend, Ind., Secretary.

American Surgical Association, Cincinnati, May 13-14. Dr. Warfield M. Firor, Johns Hopkins Hospital, Baltimore, Secretary.

Arizona State Medical Association, Tucson, April 30-May 1. Dr. Frank J. Milloy, 112 North Central Avenue, Phoenix, Secretary.

Arkansas Medical Society, Little Rock, April 19-20. Dr. W. R. Brocksher, 602 Garrison Ave., Fort Smith, Secretary.

California Medical Association, Los Angeles, May 2-3. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

Connecticut State Medical Society, New Haven, May 25-27. Dr. Creighton Barker, 258 Church Street, New Haven, Secretary.

Georgia, Medical Association of Atlanta, May 11-14. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Illinois State Medical Society, Chicago, May 18-20. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, April 29-30. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 27-28. Dr. W. Houston Toulson, 1211 Cathedral St., Baltimore, Secretary.

Massachusetts Medical Society, Boston, May 24-26. Dr. Michael A. Tighe, 8 Fenway, Boston, Secretary.

Minnesota State Medical Association, Minneapolis, May 17-19. Dr. B. B. Souster, 493 Lowry Medical Arts Bldg., St. Paul, Secretary.

Mississippi State Medical Association, Jackson, May 11-13. Dr. T. M. Dye, Clarksdale, Secretary.

Missouri State Medical Association, St. Louis, April 18-20. Mr. Raymond McIntyre, 634 North Grand Blvd., St. Louis, Executive Secretary.

National Tuberculosis Association, St. Louis, May 5-6. Dr. Charles J. Hatfield, 7th and Lombard Sts., Philadelphia, Secretary.

New Hampshire Medical Society, Manchester, May 11. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Newark, May 25-26. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, Buffalo, May 3-6. Dr. Peter Irving, 292 Madison Ave., New York, Secretary.

North Carolina, Medical Society of the State of, Raleigh, May 10-12. Dr. Roscoe D. McMillan, Red Springs, Secretary.

North Dakota State Medical Association, Bismarck, May 10-11. Dr. L. W. Larson, 221 Fifth Street, Bismarck, Secretary.

Oklahoma State Medical Association, Oklahoma City, May 11-12. Dr. Lewis J. Moorman, 210 Plaza Court Bldg., Oklahoma City, Secretary.

Rhode Island Medical Society, Providence, June 2-3. Dr. William P. Buffum, 122 Waterman St., Providence, Secretary.

Texas, State Medical Association of, Fort Worth, May 3-6. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

West Virginia Medical Association, Charleston, May 17-18. Mr. Charles Lively, 1031 Quarrier St., Charleston, Executive Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Fifteenth Annual Meeting, held in Chicago, Nov. 6 and 7, 1942

The President, DR. ARLIE R. BARNES, Mayo Clinic, Rochester, Minn., Presiding

(Continued from page 1246)

Effect of Pectin on the Coagulation of Blood in Thrombocytopenic Conditions

DR. RAPHAEL ISAACS, Chicago: Citrus pectin in the form of powder taken by mouth (in capsules) in doses of 1 Gm. three times a day, one half to one hour before meals, has been used in 8 cases of thrombocytopenic purpura over periods of from three months to one year. Two cases were of the "idiopathic thrombocytopenia" type, 2 were secondary to sulfanilamide and sulfathiazole poisoning, 2 of leukemia and 2 others of aplastic anemia. In all these cases there was a cessation of bleeding from the mucous membranes (nose, mouth, uterus) in from twelve to twenty-four hours. The coagulation time of the capillary blood was reduced to less than one minute and the bleeding time lowered to normal. There was rapid, but only incomplete, clot retraction. There was no change in the number of platelets that could be attributed to the medication. In certain nonthrombocytopenic patients with a tendency to bleed (following extraction of the teeth, menorrhagia) there was a prompt clinical response. No toxic symptoms were noted from much larger doses than those given routinely. While remissions are common in purpuric conditions, in these cases cessation of clinical bleeding was noted even though the platelet number was below 30,000 per cubic millimeter.

DISCUSSION

DR. S. C. WERCH, Chicago: My associates and I have been able to investigate the effect of pectin on coagulation. Pectin in a 2 per cent solution was injected intravenously in the in vivo experiments and was added to serum and the like in the Quick system in the in vitro experiments. No effect was ascertained. Since for all practical purposes pectin is completely destroyed in the alimentary tract and since we have not been able to show any effect on coagulation, Dr. Isaacs's observations do not appear valid to us at this time. If he had given pectin intravenously, his results might be explained by the size of the pectin molecule and blocking of the capillary walls. However, since pectin was given orally, the results can be explained only by an unknown substance which may be present in the crude preparation employed.

DR. C. J. WATSON, Minneapolis: The available evidence indicates that in thrombocytopenic purpura the main fault is in the platelet-capillary relationship: the clotting mechanism is not concerned in the production of petechiae. In a study of this sort it would be valuable to know more about capillary resistance. In other words, was the capillary resistance improved? Did the cuff test become negative after the administration of pectin? The same questions might also apply to conditions associated with hypoprothrombinemia, as for example in some cases of jaundice and frequently in sprue. There is usually a positive cuff test in cases exhibiting a hemorrhagic tendency. It would be helpful to have objective data with respect to capillary resistance in a study of this sort.

DR. RAPHAEL ISAACS, Chicago: In our cases the capillary blood clotted quickly and there were clinical remissions. As I understand it, Dr. Werch's observations were on the prothrombin time of dogs and normal men, while our observations were on the capillary blood coagulation time of patients with thrombocytopenic purpura. It has been reported that the injection of pectin solutions into dogs prolongs their coagulation time. In animals the prolonged coagulation time produced by heparin injections can be neutralized by injection of pectin. Pectin does not hasten the coagulation of blood in vitro. In 3 of the patients with pronounced capillary fragility the number of petechiae appearing after the tourniquet test was greatly reduced after pectin therapy.

"Demerol": Clinical Observations

DRS. HANS HECHT, PAUL H. NOTH and F. F. YONKMAN, Detroit: One hundred and eleven patients suffering severe pain were treated with "Demerol" (the ethyl ester of 1-methyl-4-phenyl-piperidine-4-carboxylic acid). About 75 per cent received an average of 1 Gm. over an average period of six days. The remainder received larger total amounts over longer periods up to two hundred and eleven consecutive days. The patients were suffering from a variety of acute and chronic diseases, such as arthritis, pleurisy, far advanced carcinoma, hypothalamic lesions (with so-called intractable pain), peptic ulcer and angina pectoris. Twelve patients had been receiving morphine or its derivatives from thirty to one hundred and seven days prior to administration of Demerol. The drug was administered orally or intramuscularly in doses of 0.05 to 0.10 Gm. from one to eight times daily. One patient received nine hundred and seventy-six injections. The drug was considerably more effective when given intramuscularly. Approximately 80 per cent of the patients obtained satisfactory relief of pain. The degree and duration of the analgesic effect exceeded that of 0.07 to 0.10 Gm. of codeine sulfate but was usually less than that of 0.01 Gm. of morphine sulfate.

Dizziness, nausea, vomiting, a choking sensation, momentary excitation, euphoria, dryness of the mouth and urticaria were occasionally noted immediately following administration, but in only 5 per cent of all cases were these reactions severe enough to necessitate withdrawal of the drug. Regular urinalysis, blood counts, electrocardiograms and liver function tests showed no alterations which were not explained by the disease from which the patient suffered. A firm, nontender induration of the subcutaneous tissues around the site of injection was frequently observed when the drug was given six to eight times a day over a long period of time.

After prolonged intramuscular administration (0.1 Gm. six to eight times daily for periods exceeding one month) sudden withdrawal occasionally resulted in nausea, violent vomiting, profuse perspiration, itching of the skin, irritability, depression and apprehension. These symptoms began a few hours after the drug had been withdrawn and generally lasted for one or two days. During these periods of withdrawal the patients were kept free from pain by various opiates. These reactions could easily be overcome by the use of barbiturates and scopolamine. Symptoms of this kind were never observed following prolonged oral medication.

Demerol, a synthetic substance, is apparently capable of replacing morphine and its derivatives to a certain extent, thus helping to relieve a possible future shortage of opiates. Demerol is not toxic even when given in large doses over a prolonged period. Occasional side effects are observed, and long continued use may be followed by undesirable symptoms on withdrawal.

DISCUSSION

DR. FREDRICK F. YONKMAN, Detroit: The authors have emphasized the chemical relation between atropine, morphine and Demerol. The new analgesic can be synthesized readily and, if future results substantiate present experiences with Demerol, this agent represents a distinct contribution to the field of analgesic therapy. Our attention has been directed to the spasmolytic action of Demerol and our results reveal interesting effects of the drug on certain smooth muscle. Pharmacologic studies indicate that relaxed smooth muscle may frequently be stimulated by Demerol, whereas spastic or activated visceral muscle is usually relaxed by this agent. Should the former condition occur, the analgesic action might be of sufficient degree to obviate complaint of discomfort, whereas early and rather complete relief might be anticipated if visceral relaxation with analgesia prevailed.

DR. JOHN W. SCOTT, Lexington, Ky.: It seems that a more accurate measure of relief from pain should be used in making a comparative study such as this, such a method as the Wolff-Hardy apparatus would supply.

DR. PAUL H. NOTH, Detroit: No objective method of measuring the analgesic effect was used. The Wolff-Hardy technic provides a standard pain stimulus and is useful in measuring time of onset, degree and duration of analgesic action. Such studies have been made comparing Demerol with other analgesic drugs. In our study a variable clinical painful stimulus was already present, making the Wolff-Hardy test inapplicable. Therefore the subjective response of the patient was the best measure, under these circumstances, of the effectiveness of the drug.

Treatment of Migraine With Potassium Thiocyanate

DRS. E. A. HINES JR. and L. M. EATON, Rochester, Minn.: In treating a group of patients who had hypertension with potassium thiocyanate, it was noted that many were relieved of their migraine.

Following the observation of the effect of potassium thiocyanate in relieving migraine associated with hypertension, it seemed logical to try the effect of this drug in treating a group of patients who had severe and frequent migraine attacks but who did not have hypertension. To date 27 patients have been treated for periods of three months or longer. In 2 cases it was impossible to obtain a concentration in the blood greater than 2 mg. of potassium thiocyanate per hundred cubic centimeters even though as much as 20 grains (1.3 Gm.) daily was given. After one month's trial the attempt was discontinued. Neither of these patients noted any change in the frequency or severity of the headaches. Of the group of 27 patients in whom satisfactory blood thiocyanate levels (6 to 12 mg.) could be maintained, all received some definite relief. In the majority the frequency of the headaches was reduced by 75 per cent. In 7 cases the blood cyanate level was allowed to fall to less than 1 mg. per hundred cubic centimeters without the patient's knowledge and there was a definite increase in the frequency of the attacks with subsequent relief when the blood cyanates again reached a satisfactory therapeutic level (6 to 12 mg.).

In none of our patients were there any serious toxic manifestations from the drug. It is recognized that potassium thiocyanate is a potentially dangerous drug and in our opinion it should not be used unless the dosage is controlled carefully by frequent determinations of the blood cyanate content.

DISCUSSION

DR. EDWARD MASSIE, St. Louis: I should like to ask about the intravenous injections of the drug to patients during the stages of nausea and vomiting.

DR. E. A. HINES JR., Rochester, Minn.: We have not given potassium thiocyanate intravenously, so we do not know the effect. I have thought of this as a possibility in aborting an attack when the patient has severe nausea and vomiting. I should like to know if any one has given it intravenously to human beings. I know it has been given to animals.

Organic Heart Disease and Electroconvulsive Shock Therapy

DR. VERNON L. EVANS, Aurora, Ill.: Since the use of electroconvulsive shock therapy was started at Mercyville Sanitarium, no patient has been refused the benefit of this treatment when it was thought to be indicated from a psychiatric standpoint. In many cases the risks taken appeared to be very great, but in a series of 302 consecutive cases there have been no deaths from the treatment. No attempt has been made to modify the severity of the convulsions by curare or other drugs.

In the group were 8 patients with presumptive to positive evidence of previous coronary occlusions. The ages of these patients ranged between 52 and 74. In 5 cases there were positive histories of previous coronary occlusions. Seven of the electrocardiograms showed definite inversion of the T waves in leads 1, 2 or 4. The eighth patient was a woman aged 74 who had a complete left bundle branch block. Although there was no history of heart disease this was taken as presumptive evidence of a previous coronary occlusion.

Three patients with auricular fibrillation were treated during the presence of this irregularity. Two of these patients had rheumatic heart disease with histories of previous attacks of decompensation. The other was a woman aged 75 with no his-

tory of heart disease or vascular hypertension. However, she did have generalized arteriosclerosis and moderate enlargement of the heart.

Two patients had hypertensive heart disease as shown by elevated blood pressures (210-180 systolic and 100-90 diastolic) and pronounced left axis deviation on the electrocardiogram. Two patients had probable coronary artery disease, because in 1 the PR interval was 0.23 second and in the other there was flattening of the T waves in all four leads. (There was no evidence of myxedema, and the basal metabolic rate was normal.)

With one exception no complications whatever were encountered in the treatment of these patients. The exception was a woman aged 40 who had rheumatic heart disease and a history of one previous episode of decompensation. This patient developed decompensation under treatment and the course of treatment had to be stopped after the tenth convulsion. However, the ascites and edema cleared up with the administration of diuretics and she was given no further shock treatment, as she recovered from her psychosis.

DISCUSSION

DR. A. E. BENNETT, Omaha: Most of the depressions in which we get the best results from shock therapy occur in the upper age group. Here the question of cardiovascular complications frequently arises. Dr. Evans has shown us that this treatment can be given in the presence of severe heart disease. I have treated many patients in the presence of extreme hypertension and with severe myocardial disease. However, I think a word of caution should be left with respect to this paper because it does carry the implication that the treatment is not serious. Most of the deaths that have occurred with electrotherapy have been coronary deaths. I had one such death occur two hours after an electroshock treatment. I am sure Dr. Evans would want us to explain to the relatives of the people to be treated that there is increased risk. Even though we are successful in a large percentage of depressions complicated with organic heart disease, I am sure it increases the hazard.

DR. L. N. KATZ, Chicago: This report is important because it seems to indicate that we have been too conservative in our views. A number of patients at the Michael Reese Hospital have been referred from the psychiatric department for electrocardiograms before shock therapy. A number of cases with ST depressions in the limb leads were noted for which no organic cause could be ascribed. It is possible that in psychiatric patients the ST depression sometimes may be on the same basis as the ST depression in normal people associated with fear. Thus there may be abnormalities in the electrocardiogram which are purely functional and not related to organic heart disease.

DR. CARROLL W. OSGOOD, Wauwatosa, Wis.: At the Milwaukee Sanitarium we have treated in the neighborhood of 250 cases by electric shock therapy and we feel that the treatment is relatively safe. We have treated a number of patients with electrocardiograms which are suggestive of some coronary disease. We treated one man, aged 67, who had a definite history of a coronary attack several months before. He had severe pain and had been in bed for six weeks. At the time we saw him his electrocardiogram was relatively normal. We saw no ill effects whatever from the treatment. His depression cleared up. He later had a recurrence. Altogether he had three courses of electroshock treatments, about eighteen shocks altogether. We have also treated a number of people with essential hypertension who had pressures of over 200 systolic and 100 diastolic, with no ill effects. We had one death in our series, the patient being an elderly man with some arteriosclerosis. He died suddenly immediately after the shock. An autopsy was held and no abnormality was found on examination of the heart or brain. However, there was a considerable amount of semifluid contents in the stomach, and material having the same appearance in the bronchial tubes. This emphasizes the danger of aspiration.

DR. VERNON L. EVANS, Aurora, Ill.: I did not want to imply that this treatment should be given promiscuously. I think that if we continue to give the treatment to patients who are in poor physical condition we shall have deaths. However, as yet we have had none, and it appears that the rate will be small and should not deter us from our efforts to cure people who are seriously ill.

Blood Pyruvic Acid Following Exercise in the Trained and Untrained Individual and in Patients With Heart Disease and Hypertension

DR. ZALE A. YANOF, Chicago: It is now firmly established that pyruvic acid, and not lactic acid, is the center core of tissue carbohydrate metabolism. This displacement of lactate by pyruvate stimulated this work.

A light standard exercise of fifty ascents in fifty seconds over a two-step contrivance with blood pyruvates at rest and at ten and sixty minutes after the exercise was performed on 11 collegiate wrestlers and track men, 10 sedentary individuals, 10 patients with heart disease of class II-III with enlargement of the heart and 9 class I hypertensive patients without enlargement of the heart but with blood pressures exceeding 200.

Ten minutes after the exercise the mean pyruvate change in the trained group was —5.82 per cent of that of the resting levels, the heart patients +45.75 per cent, the untrained +53.38 per cent, and the hypertensive +63.38 per cent. This difference in the utilization of carbohydrates in the "trained" individual, as opposed to that of the individual whose heart only is working overtime, suggests a clue to the complex chemical changes of "training" and "compensation" and may furnish an index of physical fitness.

The sixty minute mean pyruvate change of the trained group was —15.11 per cent of the resting level, that of the untrained group —5.82 per cent, the hypertensive 0, and the heart patients +16.66 per cent. The order of progression from negative to positive sixty minute changes is more or less in keeping with the cardiac function of these groups. This test could presumably be used to follow the course of a patient with heart disease. This is further supported by the fact that the class III heart patients with the poorest cardiac function had the highest positive sixty minute changes.

Lactate increases only after strenuous exercise, whereas in this work pyruvate changed after only light exercise as much as 100 per cent. In addition pyruvate sixty minute changes are more pronounced and circumscribed than lactate sixty minute changes. Pyruvate estimations would appear to be of value in the study of exercise physiology of both trained and untrained individuals and of patients who are not capable of undertaking the strenuous exercise that lactate requires.

DISCUSSION

DR. SAMUEL SOSKIN, Chicago: The author expresses all his results in terms of percentage changes. There should be some mention of the absolute values of pyruvic acid with which he was dealing. I should like to ask that these values be given, because I believe that they amount to only a few milligrams per hundred cubic centimeters. In view of this and the inherent errors in sampling and in chemical methods, it is not surprising that the author's data for trained and untrained subjects and for normal and pathologic individuals overlap to a considerable extent. I believe the author also ignores a known physiologic fact when he assumes that the level of pyruvate in the blood is an index of the deficiency of oxygen in the heart and skeletal muscles. It is true that when oxygen is deficient the muscles liberate excessive amounts of pyruvate and lactate into the blood, but it is also true that the normal liver rapidly removes these substances from the blood. The blood level is therefore merely the resultant of these two opposite processes. The slightly higher level of pyruvate and lactate in the blood of patients with heart disease is just as likely to result from some passive congestion of the liver as from any abnormal process in the muscles.

DR. ZALE A. YANOF, Chicago: There is some truth in all of the things Dr. Soskin said. All I attempted to do was to show what I actually found.

(To be continued)

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

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Low Spinal Anesthesia. J. E. Cameron, Alexander City.—p. 193.
Dilantin Sodium Therapy in Deteriorated Epileptics Refractory to Other Treatment. S. A. Peoples and A. F. Tatum, University.—p. 197.
Benign Ovarian Tumor, with Bilateral Hydrothorax and Ascites: Report of Case. W. N. Jones, Birmingham.—p. 199.
Management of Third Stage of Labor. R. C. Benson, Birmingham.—p. 203.

American Journal of Medical Sciences, Philadelphia

205:1-156 (Jan.) 1943

Administration of Sulfonamide Microcrystals by Inhalation. T. N. Harris, Harriet E. Sommer and C. C. Chapple, Philadelphia.—p. 1.
Medication by Chewing Sulfadiazine and Other Drugs Incorporated in Paraffin Base: Preliminary Report. J. H. Arnett, Philadelphia.—p. 6.
*Effect of Iron on Hemoglobin Regeneration in Blood Donors. Adelaide P. Barer and W. M. Fowler, Iowa City.—p. 9.
Clotting Action of Fer-de-Lance Venom. G. L. Kauer, R. M. Bird and P. Reznikoff, New York.—p. 16.
Critical Study of Action of 3-3'-Methylene-Bis-(4-Hydroxycoumarin) (Dicoumarin). C. S. Davidson and Harriet MacDonald, Boston.—p. 24.
Six Autopsied Cases of Disseminated Lupus Erythematosus. Connie M. Guion and Elisabeth C. Adams, New York.—p. 33.
*Rheumatoid Arthritis and Rheumatic Heart Disease in Autopsied Cases. T. B. Bayles, Boston.—p. 42.
Role of Heart Disease in Psychoses of the Senium. S. R. Rosen, Greenwich, Conn., and K. L. Smith, Cambridge, N. Y.—p. 48.
Extreme Tachycardia: Report of Nonfatal Paroxysms Following Myocardial Infarction. J. Edeiken, Philadelphia.—p. 52.
Family History in Arterial Hypertension: Study of 4,376 Insurance Examinations. R. H. Feldt and D. E. W. Wenstrand, Milwaukee.—p. 61.
Effect of Antipressor Kidney Extract, Angiotonin, Methylguanidine and Tyramine on Cardiac Output as Measured by Ballistocardiograph in Hypertensive and Normal Persons. R. D. Taylor and I. H. Page, Indianapolis.—p. 66.
Effect of High Fat Test Meal on Blood Cholesterol in Normal and Obese Individuals. E. Oppenheim and M. Bruger, with assistance of S. Member, New York.—p. 77.
Leukocytosis Induced by Methyl Acetamide with P-Chloroxylenol: Chemotactic Effect on Bone Marrow. B. Zondek and Y. M. Bromberg, Jerusalem, Palestine.—p. 82.
Liver Function in Therapeutic Malaria. I. Kopp and H. C. Solomon, Boston.—p. 90.
Clinical Experience with Water Soluble Vitamin K-like Substance: (Tetrasodium 2-Methyl-1, 4-Naphthohydroquinone Diphosphoric Acid Ester). J. G. Allen, Chicago.—p. 97.
Water and Electrolyte Distribution in Diabetes Mellitus: Dehydration in Diabetes. F. W. Sunderman, Philadelphia.—p. 102.
Familial Cretinism: Two Brothers Exhibiting Thyroid Deficiency and Epiphysial Dysgenesis. I. P. Bronstein, L. E. Bower and J. Murphy, Chicago.—p. 114.
Postoperative Achylia Pancreatica: Fat and Protein Absorption With and Without Replacement Therapy: Report of Case. M. Lake, N. W. Cornell and H. E. Harrison, New York.—p. 118.
Note on Evaluation of Privine Hydrochloric Acid as Nasal Vasoconstrictor. N. D. Fabricant and O. E. Van Alyea, Chicago.—p. 122.
Use of Hexene-Ol in Burns of Limited Areas. B. Levine, Cleveland.—p. 125.

Effect of Iron on Hemoglobin Regeneration in Blood Donors.—To determine the average time required for the hemoglobin to return to its original level in blood donors Barer and Fowler gave an iron salt to 89 donors after their second blood donation. The rate of hemoglobin regeneration was increased by 49 per cent so that the average daily hemoglobin increase per hundred cubic centimeters of blood was 0.0772 Gm. and the recovery period was shortened to thirty-five and two-tenths days in comparison to forty-nine and six-tenths days after the first donation without therapy. Under these conditions, 93.5 per cent of the subjects regained their normal hemoglobin level within eight weeks. Iron therapy was administered continuously and some of the subjects gave as many as five donations; subsequent donations were given as soon as the hemoglobin level reached normal. In spite of the continuous iron therapy there was a gradual decline in the rate of hemoglobin formation after each donation until it was being formed at a rate which was no more rapid than it had been without iron therapy. Therefore it seemed as if iron had progressively less effect with continuous administration. There was no evidence of bone marrow exhaustion after repeated donations.

Rheumatoid Arthritis and Heart Disease in Necropsies.—At a postmortem study of the joints of 23 patients with definite rheumatoid arthritis changes Bayles observed that in 6 there were changes in the heart valve leaflets and myocardium similar to those of rheumatic fever. The microscopic lesions of 1 could be considered active and of 5 inactive. Excluding the 1 patient because of definite rheumatic fever and rheumatic heart disease in childhood, 22 per cent had rheumatic cardiac lesions. A coincidence, a relationship of rheumatic fever and rheumatoid arthritis or the possibility that the heart disease is related to rheumatoid arthritis might be inferred from the data. Since patients with rheumatoid arthritis die of some cause other than this disease, it would be safer and probably wiser to delay a final conclusion until further studies indicate which of the three foregoing situations obtains. In the clinical treatment of the patients, the author regarded the cardiac changes as a coincidence of rheumatic heart disease and rheumatoid arthritis.

Archives of Otolaryngology, Chicago

37:1-148 (Jan.) 1943

Allergic Aspect of Vasomotor Rhinitis. H. H. Gelfand, New York.—p. 1.
Certain Aliphatic Compounds as Nasal Vasoconstrictors. A. W. Proetz, St. Louis.—p. 15.
Tension Pneumothorax and Mediastinal Emphysema After Tracheotomy: General Study, with Analysis of Seventeen Cases in Series of One Hundred and Twenty-Six Tracheotomies for Acute Obstructive Infections of Larynx, Trachea and Bronchi During Past Decade. A. H. Neffson.—p. 23.
*Diagnosis and Treatment of Ménière's Syndrome. A. Atkinson, New York.—p. 40.
Bilateral Paralysis of Abductor Muscles of Larynx: Report on Seven Patients Treated by Method, Outlined by Dr. Brien T. King. L. F. Morrison, San Francisco.—p. 54.
*Neurinoma of Facial Nerve in Middle Ear and Mastoid: Report of Case. G. J. Roberts, Pomona, Calif.—p. 62.
Functional Examination of Hearing. A. Lewy and N. Leshin, Chicago.—p. 82.

Ménière's Syndrome.—Atkinson suggests two important reasons for the failure of any particular treatment to achieve its hoped for results: laxity of diagnosis and the tendency to regard Ménière's syndrome (recurring vertigo, deafness and tinnitus) as a disease *sui generis*. Cases of the syndrome can be divided into groups according to causation and each group demands its appropriate treatment. An accurate diagnosis demands a careful neurologic examination, Bárány tests, appraisal of the relative patency of the eustachian tubes, a thorough general examination to determine the presence of any associated condition, and, when the diagnosis is still not made, idiopathic Ménière's disease is thought of instead of looking for two or more syndromes. This large remaining group of cases can be divided into at least two divisions, each with a different cause. Some may have an allergic basis and the others, about four fifths of the total, may be insensitive to histamine; that is, in these the mechanism is primarily vasoconstrictor in contrast to vasodilator of those with an allergic basis. Classification, according to the etiologic basis, which is tentative and expresses present knowledge, is as follows: A. Lesions interfering with the function of the eighth cranial nerve because of (1) lesions of the cerebellopontine angle and (2) degenerative vascular disease. B. Lesions interfering with the function of the labyrinth because of (1) alteration in intralabyrinthine pressure (*a*) from without, stricture of eustachian tube, and (*b*) from within,

increased production of endolymph (primary vasodilatation, allergy, sensitivity to histamine), (2) vascular disease: (*a*) angiospasm; primary vasoconstriction and (*b*) arteriosclerosis, and (3) "toxic labyrinthitis," that is focal infection.

Neurinoma of Facial Nerve in Middle Ear and Mastoid.—The thirteenth case of neurinoma of the facial nerve, a rare but clinical entity, is reported by Roberts. Such neurinomas are benign tumors and produce symptoms by extension and pressure. The first symptom is facial paralysis, followed after a period of years by deafness, chronic purulent otitis media and invasion of the mastoid. The tumor is microscopically characteristic of neurinomas or neurofibromas in general and presents a definite pathologic picture.

Journal of Pediatrics, St. Louis

21:705-842 (Dec.) 1942

Presidential Address: Function of Academy and Its Members During War and Peace. E. C. Mitchell, Memphis, Tenn.—p. 705.
Note on Penetration of Poliomyelitis Virus from Gastrointestinal Tract in Chimpanzee. H. A. Howe and D. Bodian, Baltimore.—p. 713.
Study of Premature Mortality. L. Flax, E. L. Levert and R. A. Strong, New Orleans.—p. 717.
Enzymic Therapy in Infant Feeding. W. C. Davison, Durham, N. C. —p. 727.
*Treatment of Ichthyosis with Vitamin A. H. G. Rapaport, H. Herman and E. Lehman, New York.—p. 733.
Match Test. H. Vollmer, with cooperation of H. W. Hyslop and H. V. Lomant, New York.—p. 747.
Modified or Reverse Schultz-Charlton Technic in Diagnosis of Scarlet Fever. J. D. Goldberg and J. De Hoff, Jamaica, N. Y.—p. 757.
Role of Honey in Prevention and Cure of Nutritional Anemia in Rats. M. H. Haydak, L. S. Palmer and M. C. Tanquary, St. Paul.—p. 763.
Influence of Diet on Physiologic Anemia of Infants. Katherin F. Brokaw, Margaret S. Sedam and Anne Marie Cassirer, New York. —p. 769.
*Thrombophlebitis Migrans. V. J. Birnberg and Arild E. Hansen, Minneapolis.—p. 775.
Study of Birth Weights and Ponderal Growth of Children of Tuberculous Mothers. C. A. Urquijo and M. Weissmann, Buenos Aires, Argentina.—p. 787.
Laurence-Moon-Biedl Syndrome: Report of Two Cases with Unusual Combinations of Heredofamilial Deviations. L. A. Lurie and S. Levy, Cincinnati.—p. 793.

Treatment of Ichthyosis with Vitamin A.—Because of impaired dark adaptation in their 6 patients with ichthyosis and because of the similarities between the accepted cutaneous manifestation of vitamin A deficiency and ichthyosis, Rapaport and his associates submitted them to daily oral doses of 60,000 to 200,000 international units of vitamin A for several months as a therapeutic test for cutaneous improvement. "Vitamin A, injectable," containing 100,000 international units of vitamin A and practically no vitamin D in 1 cc. of vegtable oil, was administered intramuscularly two or three times a week for several months. The use of this preparation excluded the possibility that vitamin D might have been a factor in the effects obtained. The results were favorable and all patients obtained an amelioration which they deemed worth while. After several months of therapy the texture of the thickened skin became more normal. Cracks and fissures disappeared entirely. Pruritus was also considerably diminished. The scales became thin, superficial and more widely separated. Improvement was noticeable at the end of a month of therapy and was progressive for several months while the treatment was continued, but whenever the vitamin A was withdrawn for an appreciable time the condition of the skin became worse. Dark adaptation also improved with the therapy. The basis of ichthyosis may be some hereditary disorder of vitamin A metabolism. In all but 1 of the 6 patients heredity played a conspicuous role.

Thrombophlebitis Migrans.—Birnberg and Hansen present the case of a boy of 14 whose death was definitely due to thrombophlebitis migrans. This, they believe, is the first time the condition has been described in a child. Heparinization was not successful in preventing further venous thrombus formation. Mesenteric thrombosis, the cause of death, was revealed at necropsy. Bacteriologic studies gave no clue to the underlying etiology. However, microscopic study of the eosinophilic inflammation and swelling of the intima of an involved vein suggested that some allergic phenomenon may have been associated with the clinical picture.

Kentucky Medical Journal, Bowling Green

41:1-32 (Jan.) 1943

*Virus Pneumonia: Treatment with Convalescent Blood. M. Flexner and M. L. Garon, Louisville.—p. 5.
Report of Case of Ruptured Intervertebral Disk Following Chiropractic Manipulation. E. D. Fisher, Murray.—p. 14.
Rural Lying-In Hospital. H. H. Caffee, Oneida.—p. 15.
Management of Rabies Contacts. G. F. Brockman, Greenville.—p. 21.

Convalescent Blood for Virus Pneumonia.—Flexner and Garon believe that their use of whole blood or plasma from convalescent donors for the treatment of 7 patients with atypical (virus) pneumonia definitely reversed the trend of the disease and shortened the convalescence. The response seemed to be specific. They reserved its use only for the seriously ill. They believe that small injections of convalescent serum or plasma might act prophylactically as does measles convalescent serum or whole blood injection in poliomyelitis. In the absence of specific donors, blood transfusion from adults may prove beneficial.

Maine Medical Association Journal, Portland

34:1-24 (Jan.) 1943

Treatment of Burns. H. Brinkman, Farmington.—p. 1.
Freudian Theories: Section II. Historical. I. Newman, Augusta.—p. 4.

Medical Annals of District of Columbia, Washington

12:1-42 (Jan.) 1943

Medicine in the Nation's Capital—1817-1942. A. C. Christie, Washington.—p. 1.
Brief Outline of Present Day Concepts of Rheumatic Fever. B. J. Walsh, Washington.—p. 9.
Some Wartime Obstetric Problems. H. F. Kane and C. K. Fraser, Washington.—p. 12.
Treatment of Puerperal Infection. R. Brown, Washington.—p. 15.
Geriatrics in Wartime. E. J. Stieglitz, Bethesda, Md.—p. 19.

Michigan State Medical Society Journal, Lansing

42:1-80 (Jan.) 1943

Preventive Aspects of Maternal Mortality. P. F. Williams, Philadelphia.—p. 25.
*Pregnancy Complicated by Acute Anterior Poliomyelitis. J. W. Peelen, Kalamazoo.—p. 30.
Achlorhydria and Gastrointestinal Disturbances: Value of Substitution Therapy. I. D. Fagin, Detroit.—p. 36.
Blindness in Michigan: Survey. J. O. Wetzel, Lansing.—p. 39.
Ideal Obstetrics. J. H. Beaton, Grand Rapids.—p. 48.
Transplantation of Preserved Tissue in Ophthalmic Surgery. M. Wiener, St. Louis.—p. 53.

Pregnancy Complicated by Poliomyelitis.—Peelen suggests that pregnancy and acute anterior poliomyelitis probably occur more frequently than a review of the literature indicates. The 29 cases reported in some detail are reviewed and 2 new ones are added. In addition 28 cases have been reported incompletely. The important conclusions are that the usual course of pregnancy does not change, the type of paralysis and complications determine whether interference with the pregnancy is necessary and it has not been proved that intrauterine poliomyelitis occurs. There are only 3 cases which suggest the possibility of intrauterine poliomyelitis. Miller believes that a bilateral clubfoot in 1 was not the result of intrauterine poliomyelitis but rather a congenital deformity, and in the other 2 the data available are insufficient to confirm or refute the possibility of intrauterine infection.

New England Journal of Medicine, Boston

228:39-80 (Jan. 14) 1943

History and Discovery and Isolation of Male Hormone. G. J. Newerla, Albany, N. Y.—p. 39.
Military Discharge for Inadequacy: Report of 182 Cases. D. J. Flicker and O. H. Coleman, Camp Blanding, Fla.—p. 48.
Gynecology: Neoplasms of Ovary. J. V. Meigs, Boston.—p. 52.

New Jersey Medical Society Journal, Trenton

40:1-40 (Jan.) 1943

Treatment of Compound Fractures in Wartime. I. E. Deibert, Camden. —p. 12.
Syphilis of Larynx. E. L. Wood, Newark.—p. 15.
Historical Sketch of Tuberculosis. B. L. Gordon, Atlantic City.—p. 17.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Clinical Science, London

4:341-448 (Dec. 15) 1942

Edema Following Ischemia in Rabbit's Ear. E. E. Pochin.—p. 341.
*Swelling of Human Limbs in Response to Immersion in Cold Water. T. Lewis.—p. 349.
Trousseau's Phenomenon in Tetany. T. Lewis.—p. 361.
Observations on Vascular Axon Reflex in Human Skin as Exhibited by Case of Urticaria, with Remarks on Nocifensor Nerve Hypothesis. T. Lewis.—p. 365.
Measurement of Duction Movements of Eye. F. F. Rundle and C. W. Wilson.—p. 385.
Assay of Renin in Rabbits with Experimental Renal Hypertension. G. W. Pickering, M. Prinzmetal and A. R. Kelsall.—p. 401.
*Experimental Trinitrotoluene Poisoning: Effect of Diet. H. P. Himsworth and L. E. Glynn.—p. 421.

Edema Produced by Cold.—The routine cooling of human hands (and feet) by their immersion in water at 41 F., Lewis observed, causes the extremities to swell. This increase in their volume occurs in both the cutaneous and subcutaneous tissue and may amount within three hours to as much as 15 per cent of the original volume. The swelling is due mainly to an edema of the tissues, judged to be inflammatory from its relatively rapid outpouring and from its relatively high content of protein. The contribution in the form of imbibed water is slight. From this and correlated evidence it seems that cold directly injures the cutaneous and subcutaneous tissue. This effect begins at about 59 to 64.4 F. and increases as the temperature of water descends. The edema that results from long continued immersion of the limbs in cold water should be taken into account, as should protein loss, when the effects of exposure to cold on the whole circulation are estimated.

Diet and Trinitrotoluene Poisoning.—In an effort to modify the seriousness of the illness that follows exposure to trinitrotoluene, Himsworth and Glynn fed white Wister rats different diets. They observed that typical necrosis of the liver and a profound, though not aplastic, anemia occurred in rats exposed to trinitrotoluene when they were on a diet rich in fat, while in animals on a high carbohydrate or a high protein diet the ill effects were slight or absent. Chronic trinitrotoluene poisoning in rats was characterized by loss of weight, increased appetite, urinary excretion of high concentrations of trinitrotoluene derivatives, a great decrease in hemoglobin, normoblasts, reticulocytes and polychromatic erythrocytes in the peripheral blood, erythroblastic hyperplasia of the bone marrow, siderosis of the spleen, fatty hepatic infiltration to acute necrosis of the parenchymal cells and loss of hair. The evidence suggests that the effect of the high fat diet is to impede the metabolic ability of the animal to dispose of the trinitrotoluene within its tissues. The resemblance between the effects of trinitrotoluene poisoning in the rat and of that in man is close.

Lancet, London

1:1-34 (Jan. 2) 1943

Surgery in the Middle East. E. G. Muir.—p. 1.
*Cross Desensitization in Allergic Diseases. Kate Maunsell.—p. 3.
Recovery from Heart Failure After Cardiac Massage. H. K. Vernon. —p. 6.
*Accidental Head Injuries: Prognosis in Service Patients. C. P. Symonds and W. R. Russell.—p. 7.
Postcontusional Headache. E. Guttmann.—p. 10.
Method of Controlling Bronchial Secretion in Thoracic Surgery. J. Halton.—p. 12.
*Perurethral Methods in Benign Prostatic Hypertrophy. T. L. Chapman. —p. 14.

Cross Desensitization in Allergic Diseases.—Maunsell deals with desensitization to the class of allergens called idiotoxins or atopens which cause bronchial asthma, eczema, conjunctivitis and rhinitis. The allergic properties are exerted by food proteins, pollen and other constituents of plants, animal feathers, hair and wool, dust, bacteria and mold. Her investigation is designed to examine the specificity of the antiallergic mechanism, for which a method of local desensitization of the skin has been studied. The technic was applied to obtain evidence whether in multisensitive patients one allergen can desensitize the skin so that it will no longer react to the others. This is termed "cross desensitization" as opposed to the "direct desensitization," in which the same allergen is used for desensitizing and retesting. If the desensitization is carried out with two allergens of the same cutaneous activity a reciprocal cross desensitization occurs. If one allergen is stronger than the other the desensitization is unilateral. The occurrence of either reciprocal or unilateral desensitization is independent of the biologic group of the allergens. The desensitization is only a quantitative change and not a qualitative return to a normal response. Observations on the histamine reaction in desensitized areas showed that the decrease in the allergic reaction is not a mere general refractoriness of the tissues but the result of an antiallergic mechanism. The wide range of cross desensitization suggests that a patient with a multiple sensitiveness does not require a mixed extract but that treatment with a single allergen is sufficient. If various allergens give equally positive reactions, the extract that is obtainable in the strongest concentration should be chosen, so that during treatment the initial dose can be increased ten thousand times or more. An improvement in desensitization must not be expected from finding still more skin-reacting allergens but from the production of highly effective extracts and by carrying the densitization as far as possible.

Accidental Head Injuries.—In the course of their work at a military hospital for head injuries Symonds and Russell dealt with a variety of head injuries due to accidents of a kind that also occur in civil life. Their series of 242 acute consecutive cases is not entirely representative of accidental injuries because it does not include those cases in which the severity of the head injury or associated injuries of other parts forbade transfer within three weeks. This explains the low mortality; there were five deaths, and 22 (9 per cent) of the survivors were invalided out of the service. The others, 215, or 89 per cent, were returned to duty. A follow-up showed that a further 11 per cent were invalided later. A long post-traumatic amnesia carried a relatively bad prognosis for return to duty. Analysis of those returned to duty and followed up shows that in 90 per cent treatment (including rehabilitation) was less than three months; there was no difference in the length of treatment between those who had a relapse and those who remained well. The return to duty of 718 patients with chronic head injury, largely selected for admission to a special hospital because of unsatisfactory progress, was more than twice as bad as for the acute cases. There was a correlation between this bad prognosis and a higher incidence in this group of predisposition to mental disorders. The prognosis for return to duty among 111 personnel of the Royal Air Force with acute and chronic head injuries was four times as good as in the total series. The main reason for this relatively good prognosis in flying personnel probably was due to the fact that they were a highly selected group in respect to the absence of a predisposition to mental disorders.

Perurethral Methods in Benign Prostatic Hypertrophy.—Chapman has employed perurethral prostatic resection with the Thompson resectoscope since 1938. His results in 100 consecutive cases have been far short of those obtained at the Mayo Clinic. It is chiefly in the benign group that the choice between suprapubic and perurethral methods arises. Six of the 100 men died; in 93 of the 94 survivors urethral micturition was achieved; the 1 patient in which this failed was mentally deteriorated. Micturition was sluggish in 10, and 4 of these were advised to continue with suprapubic drainage. In 3 there was evidence of recurrence of obstruction and in 2 others this was suspected. Function was maintained in the rest. The follow-up period extended up to four years. One instance that was clinically benign at operation later became malignant. Suprapubic prostatectomy offers little or no advantage over a perurethral prostatectomy in the removal of early foci of a malignant condition. Incontinence rarely occurred, and then it responded to treatment.

Tubercle, London

23:215-238 (Oct.) 1942

Some Observations on Effects of Experimental Diets on Pulmonary Tuberculosis. G. Day.—p. 215.
Aspiratory Metastasis. E. Fraenkel.—p. 227.

Gastroenterologia, Basel

66:121-248, 1941-1942. **Partial Index**

Alimentary Idiosyncrasy. E. Hanhart.—p. 121.
Abdominal Meteorism. R. M. Tecoz.—p. 130.
Meteorism: Its Roentgenologic Aspects and Their Diagnostic Value in Some Intestinal Diseases. O. Walther.—p. 162.
Osteomalacia and Hypochromic Anemia After Gastric Resections. Charlotte Sarasin.—p. 182.
*Anemia in Kyphoscoliosis. F. Reimann.—p. 197.

Anemia in Kyphoscoliosis; Hemorrhagic Gastritis.—Reimann reports 4 cases of severe kyphoscoliosis associated with hypochromic anemia caused by profuse gastrointestinal hemorrhages. Examination of the stomach of 1 patient following resection revealed extensive erosions of the mucosa as the anatomic basis of the gastropathy. The gastric disorder has a causal relationship to the kyphoscoliosis in that the latter produces abnormal spatial conditions. There is a compression of the stomach and duodenum, delayed emptying of the stomach, a tendency to frequent vomiting, compression of the large abdominal vessels at the root of the mesentery and interference with circulation in the gastric vessels. Delayed emptying and stasis in the gastric vessels cause gastric symptoms and severe hemorrhages. These symptoms disappear in the reclining position and recur when the patient gets up; they have a distinct orthostatic character. The symptoms kyphoscoliosis, hypochromic anemia and erosive hemorrhagic gastropathy are a pathogenic triad which can be designated as "anemia in kyphoscoliosis." Knowledge of this syndrome is important in the evaluation of gastric disorders in patients with kyphoscoliosis.

Schweizerische medizinische Wochenschrift, Basel

72:909-932 (Aug. 22) 1942. **Partial Index**

Therapeutic Results in Cervical Cancer. J. H. Müller.—p. 909.
*So-Called Interstitial Plasma Cell Pneumonia in Early Infancy. F. and W. Stirnimann.—p. 910.
Cecal Invagination in Regional Enteritis (Terminal Ileitis). G. Rieben.—p. 914.
Experiences with Insulin in Schizophrenia. A. Friedemann.—p. 916.
*Serodiagnosis of Undulant Fever: Advantages of Complement Fixation. V. Badoux.—p. 920.
Allergic Myocarditis and Nephritis in Case of Tuberculous Hilar Adenitis. J. Flagg and M. Froehner.—p. 922.

Interstitial Plasma Cell Pneumonia in Infancy.—The Stirnimanns report observations on cases of interstitial plasma cell pneumonia. An alarming increase became apparent in the fall of 1941. Five infants developed the disorder in short succession and 4 of them died, while of the earlier cases about half had recovered. It was surprising that all children who developed this form of pneumonia had been in the same room. Moreover, 1 infant who had been nursed in this room developed interstitial plasma cell pneumonia six weeks after discharge from the hospital. Necropsy of the 4 children who died last verified the diagnosis of interstitial plasma cell pneumonia. The authors observed in all 14 typical cases and a few atypical cases. The cases observed by them differed from others reported in that all the infants with one exception were normal, well developed and not prematurely born. The authors advance the following hypothesis regarding the still obscure pathogenesis: A neurotropic virus damages the respiratory regulation in the diencephalon so that the tonus of the inspiratory muscles, with the exception of the diaphragm, is intensified and the respiratory air is decreased. The extreme inspiratory position of the ribs dilates the pulmonary tissue, which is easily torn at this age. Thus alveolar ruptures or spontaneous pneumothorax is likely. The forced expiration together with the glottis closure increases the intrapulmonary pressure in thrusts. The tears in the alveoli lead to interstitial emphysema, which in turn leads to mediastinal and paratracheal emphysema. Not only air but also detritus is driven into these clefts, and in this way the picture of interstitial plasmocytic pneumonia results. Where the detritus originates, whether in the infection or in the torn tissue, will require further investigations. The description of the disease still has gaps, and it still presents unsolved problems which require further observations.

Serodiagnosis of Undulant Fever.—Defining the role which the laboratory should play in the serodiagnosis of undulant fever, Badoux says that the physician will demand (1) a hemoculture, (2) an agglutination test and (3) the fixation of the complement. Hemoculture will be most successful in the recent and febrile cases. Unfortunately the positive results are rare, particularly in case of Brucella abortus bovis (Bang) infection, which is most frequent in Switzerland. There remain agglutination and fixation of the complement. He made comparative studies with these two tests on 527 patients who were suspected to have brucellosis. The superiority of the fixation of the complement was demonstrated by the fact that it produced 6.45 per cent more positive reactions than did the agglutination test. In conclusion the author calls attention to the high incidence of human brucellosis, particularly Brucella abortus infection in the French speaking part of Switzerland. He maintains that the serologic methods are often the only procedures which permit a definite diagnosis and that serodiagnosis will be carried out with maximum success by (1) fixation of the complement, (2) the agglutination of Wright and (3) hemoculture.

Semana Médica, Buenos Aires

49: 941-1003 (Oct. 22) 1942. **Partial Index**

Therapy of Cancer. J. Zavala Muñiz.—p. 943.
*Pericarditis in Infants. R. Kreutzer, B. Paz and I. Diaz Bobillo.—p. 953.
Syphilis and Asthma: May Syphilis Play Any Role in Development of Asthma? J. A. Cruciani and O. E. Prada.—p. 963.
Diabetes and Postoperative Hypothyroidism. E. G. Fongi.—p. 984.

Pericarditis in Infants.—Kreutzer and his collaborators report 8 cases of pericarditis with effusion in infants (2 girls and 6 boys). A clinical and roentgen diagnosis was made in all cases. Electrocardiograms were taken in 4 cases. The disease was purulent in 6 cases and serous and serohemorrhagic in 1 case each. It was secondary to suppurative bronchopulmonary or pleuropulmonary disease in 4 cases, to suppurated cervical adenitis in 2 cases and to osteomyelitis of the clavicle in 1 case. Pain and fever were early symptoms. The constant moaning of the patients was interpreted as complaint of pain. Fever was moderate in 1 case, acute and of the septic type in the cases of purulent pericarditis and did not appear in the only case of idiopathic pericarditis. Dyspnea, cough and cyanosis appeared late in the course of the disease. The authors found that the diagnosis is made by the aforementioned symptoms and by certain physical signs and electrocardiographic changes. The cardiac sounds as heard in the four foci of auscultation may be either weak or normal. The enlargement of the area of cardiac dulness at percussion and the signs of compression of the left lower lobe of the lung by the enlarged pericardium are of pathognomonic value. The enlargement of the x-ray shadow of the heart is also of diagnostic value. The size of the shadow depends on the amount of pericardial liquid. Its form varies with the postural changes of the patient as the liquid is displaced according to the laws of gravity. Radioscopy is also of value. Pulsation of the heart may be diminished, but the so-called quiet heart is exceptionally rare. The increase of venous pressure and the consequent engorgement of the jugular veins, enlargement of the liver and development of ascites and edema depend on the more or less rapid accumulation of pericardial fluid. As a rule they follow a slow course except in cases of serohemorrhagic pericarditis, in which the pericardial liquid is rapidly collected. The changes of the electrocardiogram consist in elevation of the ST segment, especially in the second lead, and of inversion of the T wave in the four leads. The diagnosis is verified by the results of pericardial puncture. Pneumococci, streptococci and staphylococci are, in order of frequency, the bacteria found in suppurated pericarditis. The pericardial fluid does not contain bacteria in cases of idiopathic serous pericarditis. The prognosis is good in idiopathic pericarditis, moderate in the serohemorrhagic form of the disease and fatal in suppurative pericarditis. The prognosis of suppurative pericarditis can be improved by early therapy consisting of pericardiotomy and administration of sulfanilamide. The patients with serous (idiopathic) and serohemorrhagic pericarditis were reported by the author cured. Four patients died from suppurative pericarditis. Two patients died from renal abscess complicating suppurative pericarditis.

Book Notices

Recent Advances in Anæsthesia and Analgesia (Including Oxygen Therapy). By C. Langton Hewer, M.B., B.S., D.A., Senior Anæsthetist, St. Bartholomew's Hospital, London. Fourth edition. Cloth. Price, $5.50. Pp. 341, with 135 illustrations. Philadelphia: Blakiston Company, 1943.

The author, who is a well known British anesthetist, has gathered from the literature (largely British) much relatively recent material. For the most part he indicates his agreement or disagreement with opinions expressed in the literature. The fields considered are theoretical aspects of inhalation anesthesia, premedication, nitrous oxide and the hydrocarbon gases, carbon dioxide and helium, modern apparatus for the administration of the gas anesthetics, recent work on the ethers, the halogen containing anesthetics, recent developments in endotracheal anesthesia, the explosion risk in anesthesia, intravenous anesthesia, general aspects of local analgesia, drugs used in local analgesia, recent advances in the technic of local analgesia, the present position of spinal analgesia, collapse and resuscitation, anesthesia for cranial and dental surgery, anesthesia for endoscopy and nasal and oral surgery and use of suction, anesthesia and analgesia for thyroid, thoracic and abdominal surgery and in obstetrics with comments on resuscitation of the newborn, anesthetic sequelae, psychologic aspects of anesthesia and analgesia and oxygen therapy. The book is especially interesting to the experienced anesthetist. It reflects the rapid advancement in anesthesiology. It is also valuable to the inexperienced anesthetist in that it serves as a guide to his reading. This small book is similar to the annual reports published in certain fields in order to record recent progress. It includes many practical points that may be applied clinically; however, many who read it will feel that they would gladly trade much of the material in the book, which has been gathered from the literature, for more information from the author on how he anesthetizes patients.

The Antigonadotropic Factor with Consideration of the Antihormone Problem. By Bernhard Zondek and Felix Sulman, Hebrew University, Jerusalem. Cloth Price, $3. Pp. 185. Baltimore: Williams & Wilkins Company, 1942.

The authors have chosen to discuss a controversial subject. The review is thorough and gives much data, pro and con, based on experimental evidence both animal and human. Historically, Long and Evans in 1921-1922 found that protracted treatment of female infantile rats with anterior pituitary extracts induced the formation of atretic corpora lutea, atrophy of the ovaries and failure of estrus. Zondek in 1930 reported that female animals subjected to prolonged treatment with gonotropic extract showed definite involution of the genital organs. In 1929 Lee, Teel and Gagnon reported failure of continued stimulation following prolonged treatment with thyrotropic factor. In 1934 Collip and Anderson postulated the presence of an antithyrotropic hormone. Since then antihormonal reactions have been reported for almost all the known hormones, especially those having a protein structure, such as the pituitary, the parathyroid, the adrenal and the pancreatic.

Zondek and Sulman state that "one of the main difficulties of antihormone research is that hormone preparations are not available 100 per cent pure. These contain the hormone together with protein contaminants . . . which compete with the hormone in serological ability to form antibodies." They conclude "We feel that the arguments presented suffice to establish the view that antiprolan formation is an immune reaction. Up to the present, only protein-containing hormones, especially the anterior pituitary (and cortin) have been found to evoke the formation of antihormones. It seems to have been proved that antihormone formation does not occur from protracted treatment with the steroid hormones, or with insulin, adrenalin, thyroid hormone (thyroxin), pitressin or pitocen. . . . The theory is here advanced, therefore, that the antigonadotropic factor represents a new type of blood substance which, though closely related to the immune bodies, does not give the in vitro reactions which generally characterize an antibody. It seems likely, furthermore, that also antifactors other than the antigonadotropic factor are immune bodies; the antigonadotropic substances in any case are not 'hormones with reverse properties'; they are immune bodies which lack a visible in vitro reaction. Their general behavior in vivo and in vitro leads to their classification as a group of immune bodies of a character hitherto unknown in serology."

While this book indicates a comprehensive knowledge of the subject "antihormones" and contains valuable information for investigators who are doing animal research, it is too complicated for the clinician. The subject is furthermore too theoretical to have practical clinical value now.

The Relation of Certain Anomalies of Vision and Lateral Dominance to Reading Disability. By Philip W. Johnston, Ph.D., Research Consultant, Mass. Dept. of Public Health, Boston. Monographs of the Society for Research in Child Development, Volume VII, No. 2 (Serial No. 32). Paper. Price, $1.50. Pp. 154, with 31 illustrations. Washington, D. C.: National Research Council, 1942.

The investigation was designed to determine the importance of various visual functions as factors in reading disability. The factors considered were visual acuity, muscle balance and anomalies of ocular dominance. A group of school children in Reading, Mass., were submitted to tests for these functions, and the results were compared with their record of reading accomplishment. The use of the various tests is accurately described. The Massachusetts vision test was used in estimating visual acuity, with certain modifications, including a method of using the Landolt broken ring test in a way which seems more practical than any yet described. Variations in this test were minimized when standardized methods were employed and when one particularly well qualified member of the school staff was employed to do all the testing. Results indicated a probable association between latent hyperopia and low reading achievement. No such relationship was found between reading disability and heterophoria as found in this group.

Ocular dominance was determined by a battery of ten tests performed on each child, and right or left handedness was determined by a similar series of tests. The results are treated in an elaborate statistical manner with profuse use of algebraic formulas and graphs, which are confusing to the reader with an ordinary medical education. Out of it all, however, comes the sober conclusion that no correlation between discongruities of ocular dominance and handedness and cases of reading disability could be found. The series in which the latter series of tests was made was not a large one, but the conclusion, if corroborated, will be of importance, since many educators, without much evidence, have placed great stress on such a probable relationship and this is perhaps the most accurately controlled series of observations which has been made on the subject.

The Biological Action of the Vitamins: A Symposium. Edited by E. A. Evans Jr., Associate Professor of Biochemistry, the University of Chicago. Cloth. Price, $3. Pp. 227, with 30 illustrations. Chicago: University of Chicago Press, 1942.

Under present conditions it probably will be a long time before such another symposium is held as the one on respiratory enzymes at the University of Wisconsin, and its sequel on the biologic action of the vitamins at the University of Chicago late in 1942. The present volume is a companion piece to the volume on respiratory enzymes published under the editorship of Prof. Perry Wilson of the University of Wisconsin. It consists of fourteen essays on the vitamins, each one being an important presentation by a distinguished investigator. The general tone of the papers is brought out in the initial paper on "The Biological Action of the Vitamins" by C. A. Elvehjem, in which he has called attention to the change in direction of research on the vitamins. Whereas much of the earlier work on vitamins involved a study of growth in animals, the present direction is toward a study of the action in tissues. Here the work has been made possible by advances in the field of enzyme chemistry and thus these two phases of biochemistry have been brought together, at least with regard to some of the members of the vitamin B complex. Thus thiamine, riboflavin and nicotinic acid in combination with other substances have been demonstrated to be essential components of enzyme systems concerned with the oxidation of foodstuffs. Ochoa has written

on cocarboxylase, Norman Jolliffe on the clinical aspects of vitamin B_1, Paul György on riboflavin deficiency in the human being, and David T. Smith on nicotinic acid and pellagra. S. Lepkovsky has contributed a brief discussion of pyridoxine, R. J. Williams has written on pantothenic acid, Edgar S. Gordon on pantothenic acid in human nutrition and Vicent du Vigneaud on biotin. Wendell H. Griffith, now on foreign service with the Army, has given an excellent presentation of the facts about choline. Franklin C. McLean has presented new points of view about the economy of phosphorus in the animal organism, and D. W. MacCorquodale and H. P. Smith and E. D. Warner have written about vitamin K. Persons interested in any one of these phases of vitamins will find this book exceedingly useful and stimulating.

Climate Makes the Man. By Clarence A. Mills, M.D., Ph.D., Professor of Experimental Medicine, University of Cincinnati. Cloth. Price, $3. Pp. 320. New York & London: Harper & Brothers, 1942.

The title of this well written book aptly characterizes the content. Designed for the nonprofessional reader, it presents a survey of the many interrelated fields in which climate assumes a role—a role much greater than the modern medical man and more particularly the modern medical scientist has cared to consider. For this very reason this popular survey, while purely nonscientific from the point of view of omitting all references to the literature, can be most useful to the physician who may still have sufficient time and detachment to think of the causes of disease as multiple rather than single.

Physicians of an earlier generation were more than conscious of this. In von Leyden's biography a chance remark on the health conditions of Bucharest is pertinent: "For despite its beautiful situation Bucharest is by no means among the healthier cities; the climate is not favorable, in winter temperatures fall to — 24 C. and during the heat of summer reach 48 C. . . . among the patients who consulted me were many with heart disease (nonrheumatic in character) . . . which leads me to conclude that the cause must be associated with the climatic conditions." Coming from the north of Europe, the more brusque and taxing changes in the weather of the Balkans and Russia impressed the medical visitor. Page Hitler for confirmation!

"Climate Makes the Man," finding favor with the reading public, will indirectly awaken the interest of the physician. Patients are living organisms that are conditioned by the weather and the climate. Their diseases reflect these changing conditions, and the physician who evaluates the sum total of the environmental factors becomes a better physician. But this is not yet taught in the medical schools.

The Vertebrate Eye and Its Adaptive Radiation. By Gordon Lynn Walls, Research Associate in Ophthalmology, Wayne University College of Medicine, Detroit. Bulletin No. 19, Cranbrook Institute of Science Cloth. Price, $6.50. Pp. 785, with 198 illustrations. Bloomfield Hills, Michigan: Cranbrook Institute of Science, 1942.

This book is the nineteenth bulletin of the Cranbrook Institute of Science, a massive tome with illustrations galore. The material deals with the various phases of the vertebrate eye. The first part is labeled "basic." It treats of light and its properties with especial reference to perception by an eye. The eye itself, the human eye, is then discussed and dissected from all points, starting with embryology, passing through the gross and microscopic anatomy, and finishing with the physiology of vision. This part is well written in plain language. The second part is the ecologic; in this are discussed the necessary adaptations that the visual apparatus has undergone and is still undergoing so that the parent organism may survive under various conditions. To the clinical ophthalmologist, much of this section will be entirely new and he will be surprised how much of this applies to his daily routine. The third section is labeled "synoptic," which Webster defines as "affording a general view of a whole or of its principal parts." In this are described the eyes and their why and wherefore of birds, beasts, reptiles and fishes. Here too the clinician will find much of interest. While this book is essentially for reference, the average thinking physician can read it with pleasure and profit. The bookmaking is good, as are the illustrations, which are largely diagrammatic and hence easily understandable.

Pesquisas sobre a febre amarela. Por el Dr. Hermínio Linhares, biologista interino do Instituto Oswaldo Cruz. Tese. Paper. Pp. 78. Rio de Janeiro: Imprensa nacional, 1941.

This is a thesis written for the degree of doctor of medicine from the University of Brazil to be considered by the faculty of that institution in the manner of and modeled after French schools of medicine. During 1939, 1940 and for a few months of 1941 the author worked in the yellow fever service of the Ministry of Education and Health of Brazil and through that organization in cooperation with the International Health Division of the Rockefeller Foundation. It seems to be a careful study of the yellow fever virus. The experimental animals used in the study were chicks, mice and cats; the primary purpose was to study passages of the virus from animal to animal, roûtes by which these animals are susceptible, organs within the body of the animals in which the virus may be found after specific periods of time, the effect on the virus of avitaminosis B and the periods of time following inoculation in which immune bodies appear, correlated with age and route of introduction. It is pointed out that following intradermal inoculation of the virus it is not impossible that infected mosquitoes may be responsible for the spread of the virus among chicks and perhaps other very young birds, which suggests a possible reservoir. The volume is bound in durable paper, written in the Portuguese language and well printed on permanent glossy paper. Comprehensive English summaries are appended to each of four sections. Included in the book are numerous well designed and informative tables and several graphs setting forth in detail the results of the experiments.

Laboratory Handbook for Dietetics. Compiled by Goodrin Thompson, Head Dietitian, Municipal Hospitals, Winnipeg, Canada, under the direction of Margaret A. Ohlson, Associate Professor Foods and Nutrition, Iowa State College, Ames, Iowa. Paper. Price, $1.25. Pp. 73. Minneapolis: Burgess Publishing Company, 1942.

This is an 8 by 11 spiral book, prepared to furnish students with convenient tables for use in evaluating diets. The table of dietary allowances contains the figures of the Committee on Foods and Nutrition of the National Research Council, May 1941. The sources from which the data quoted in the table of proximate composition of some American foods were obtained are all listed and are known to be reliable. The table is ample for ordinary use. The last fifty pages of the book are recipes in tabular form to be evaluated by the student. Its purpose is to require the student to analyze food combinations and recognize the wide difference in the proximate composition of the final product. These tables omit space for fat and carbohydrate. Moreover, an equal number of blanks for the student's own recipes would give the book broader use. Tables giving the chief food sources of each of the specific nutrients or space where the student might record these would also be of great value.

La toracoplastia ántero-lateral elástica de Monaldi. Por Jacinto Foglio. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas, Escuela de medicina. Paper. Pp. 86, with 39 illustrations. Buenos Aires: Establecimiento tipográfico de A. Guidi Buffarini, 1942.

This gives an excellent account of the indications, operatory methods and results of Monaldi's operation. The views of the Italian school—Forlanini, Morelli and Monaldi—are clearly summarized. The conclusions of the author are supported by numerous clinical histories and reproductions of x-ray plates, and the literature on the subject is thoroughly quoted.

Paginas clínicas. Por el Doctor Lazaro Mendoza h., profesor de clínica médica (semiología y diagnóstico), Universidad de El Salvador, San Salvador. Paper. Pp. 166. San Salvador: Imprenta nacional, 1942.

The author, professor of medicine in the University of Salvador, has selected 36 interesting and varied cases which range from malaria to cancer of the pancreas. A devout admirer of French medicine, he deals with his problems in a light, picturesque and yet penetrating manner. The most interesting chapters are the fourteenth, fifteenth and sixteenth, in which he comments on the first cases of typhus fever, murine type, ever described in his country.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

COLOR BLINDNESS OF PHYSICIAN AND MILITARY SERVICE

To the Editor:—**One of our boys in medical school is color blind. As I understand the military requirement, that would bar him from military service. What effect will that have on him in general practice of medicine and surgery?**

Robert H. Kerr, M.D., Alma, Neb.

ANSWER.—Color blindness is not a bar from army service in the medical corps. Those who are color blind are not acceptable for general military service but can qualify for limited military duty. It is believed to be barred in the Navy Medical Corps as it is in aviation services. It does offer certain handicaps in medical work, chiefly in certain laboratory procedures, but there are a number of physicians who are red-green blind (the common anomaly) who have done excellent work and claim to have noticed little, if any, inconvenience from this defect.

PHARMACOLOGIC EFFECTS OF YOHIMBINE

To the Editor:—**I have noted in some literature from a manufacturing pharmaceutical concern relative to the use of yohimbine that vertigo, nervous excitation, palpitation, insomnia and headache indicate a reduction or discontinuance of the remedy. With 1 patient I have noted most of the symptoms mentioned quite definite with even a small dose. Have you any data concerning the physiologic action of yohimbine on the circulatory, respiratory, nervous or other body systems which might explain the symptoms noted?**

M.D., New Mexico.

ANSWER.—The undesirable symptoms and reactions reported after yohimbine are correctly emphasized as those indicating toxicity and are apparently directly associated with a fall in blood pressure. It has been shown by Hamet (*Compt. rend. Acad. d. sc.* **93**:1274 [Nov. 27] 1925) in Europe and by Young, Yonkman and their co-workers in this country that the alkaloid and some of its derivatives produce an abrupt and pronounced fall in blood pressure, respiratory changes and occasional skeletal tremors when injected intravenously into anesthetized cats and dogs. In cats a dose of 3 to 7 mg. per kilogram produces a paralysis of salivation controlled by the cervical sympathetic nerve as demonstrated by failure of secretion when the nerve is electrically stimulated after yohimbine (Yonkman, F. F., and Young, A. G.: The Antisympatheticomimetic Effect of Ethyl Yohimbine on Salivation and Mydriasis, *J. Pharmacol. & Exper. Therap.* **63**:40 [May] 1938). This sympatholytic action, together with the well known "epinephrine reversal" effect elicited by the drug (Young, A. G., and Yonkman, F. F.: Further Studies of the Chemotherapy of Yohimbine Compounds, *ibid.* **57**:150 [June] 1936), suggested the use of yohimbine in experimental hypertension of the type produced in dogs by Page's technic of kidney envelopment. The alkaloid, when intravenously administered, is capable of acutely lowering tension and is still able to reverse the effect of epinephrine in the hypertensive state (Chase, H. S.; Yonkman, F. F., and Lehman, A. J.: The Effect of Ethyl Yohimbine in Experimental Hypertension, *ibid.* **72**:6 [May] 1941).

After oral treatment of hypertensive dogs with yohimbine it was found (Jacobs, J., and Yonkman, F. F.: The Effect of Yohimbine Hydrochloride in Trained Unanesthetized Dogs with Experimental [Page Type] Hypertension, to be published) that an initial dose of 10 mg. per kilogram produced after five to fifteen minutes profound salivation, panting, increased pulse rate, fall in blood pressure, generalized tremors and weakness to the point of collapse. The animals were evidently in real distress. However, beginning with smaller daily doses of 1 to 3 mg. per kilogram the undesirable symptoms and reactions were diminished or obviated; apparently an early tolerance seems to be developed to some extent, but pressure decline persisted as long as treatment continued for twelve months or more.

Clinically, 1 to 2 mg. per kilogram can be tolerated orally by most patients. The described side reactions should be carefully avoided if possible and one must always anticipate the hyperreactive patient such as the one described. The early treatment of essential hypertension on a sympatholytic basis seems promising, but acceptance of this procedure awaits further clinical study.

INJECTION OF HEMORRHOIDS AND OBTURATOR NERVE PARALYSIS

To the Editor:—**Are there recorded instances of bilateral obturator nerve paralyses following hemorrhoidal injections? I should appreciate knowing the best procedure or treatment used in such cases.**

M.D., Nebraska.

ANSWER.—The obturator nerve arises from the lumbar plexus by a fusion of the three anterior divisions of the plexus, which are derived from the second, third and fourth lumbar nerves. Emerging from the medial border of the psoas near the brim of the pelvis, it passes on the lateral side of the hypogastric vessels and ureter and descends through the obturator foramen to the medial side of the thigh. The symptoms of isolated paralysis of this nerve, which is rare, are impairment of external rotation and adduction of the thigh, difficulty in crossing the legs and a small, insignificant sensory loss.

Injection of hemorrhoids occasionally causes an ascending thrombosis of the superior hemorrhoidal vein. For several days the patient feels pressure and fulness in the pelvis, and to digital palpation a sensitive leathery thickening may be felt extending 2 or 3 inches upward from the site of injection. Rarely an embolus into the portal system, notably into the liver, may occur. The inferior and middle hemorrhoidal veins drain into the internal pudic and from here into the hypogastric vein. No case of obturator paralysis has been recognized from a thrombosis of the hypogastric vein, although in a septic ascending thrombosis with abscess formation one can observe radiation of pain into gluteal or sciatic territory. In order to explain a bilateral paralysis, either the obturator nerve must be involved through a bilateral hypogastric thrombosis or the block must occur in the vertebral canal into which the anterior vertebral veins may drain blood from the hemorrhoidal venous plexus.

These data are given as a basis for a possible anatomic connection between the injection of hemorrhoids and the paralysis of the obturator nerves. Whether such a connection can really be assumed would depend on data which the correspondent does not submit; namely, type of rectal lesion treated, symptoms following injection and interval between the injection and the paralysis. Other causes of paralysis, namely pressure on the pelvic brim, intrapelvic abscesses and position of the patient on the operating table, should be considered. Finally, a neurologic lesion associated with involvement of other nerves, mostly the femoral, must be thought of. Treatment cannot be suggested unless the cause of the lesion can be more closely defined.

REFRACTORY PARATYPHOID A INFECTION OF LIVER AND BILE TRACT

To the Editor:—**A man aged 29 has had an infection with paratyphoid A organisms for eighteen weeks. He has a septic type of fever, below normal in the morning and up to 104 F. every night. Every possible focus of infection except the liver and the gallbladder has been eliminated where on laparotomy small abscesses were found throughout the liver. The gallbladder itself contained bile which had numerous pus cells and paratyphoid A organisms. Have there been any reports of liver abscess complicating paratyphoid A infection or any in which drainage of the common bile duct has afforded cure? The gallbladder has already been drained, the bile flowing freely for three weeks without appreciable effect on the fever. The tube has since fallen out and drainage has ceased. While the gallbladder was draining the patient's fever was lower but since it has stopped draining his chills have returned and his temperature has resumed its high level. Sulfathiazole, sulfadiazine and azosulfamide have been tried without much effect. Sulfapyridine reduced the temperature for two days but had to be discontinued, since the patient could not tolerate it. The main question now is whether the common bile duct should be drained again and the entire bile flow redirected outside the body.**

H. D. Cheifetz, M.D., Montreal, Que.

ANSWER.—The occurrence of multiple abscesses of the liver has been observed in the typhoid infections. It is not common but is more common than solitary abscess of the liver. The multiple abscesses usually follow a suppurative cholangitis or a pylephlebitis following appendical involvement. It seems likely in this case that the primary difficulty lies in the liver, and that the gallbladder is secondarily infected. In such a situation drainage of the gallbladder would afford some relief but would not adequately drain the foci in the liver. All of this could easily account for the septic type of fever, although other foci should be sought. Thrombophlebitis elsewhere and pyelitis may cause a similar course.

It seems unlikely that further drainage of the gallbladder would effect a cure. At least other methods would seem indicated first. In such a case as this, it is necessary to grasp at straws. While sulfaguanidine therapy has not yet received sufficient support to warrant its widespread adoption, it would certainly be worth a trial. Convalescent serum has had some support in the past and would certainly be harmless. Immunotransfusion, that is, transfusion of whole blood from an immune donor, is worth consideration. If all these measures fail, surgical drainage of the biliary tract may be reconsidered.

RECURRENT ULCERS AND NEUROLOGIC DISTURBANCE OF LEG

To the Editor:—A woman gives a history of being well until two years ago, at which time she thought she hurt her left foot at the ankle and an ulcer developed soon afterward. This ulcer did not heal for several months, and soon after it did heal another developed. These ulcers have been coming and going ever since, always being somewhere on the lower part of the left leg near the ankle. At present she has a large craterlike ulcer on the inner aspect of the ankle, which has been present since July and which will not heal in spite of therapy used. She has a number of large scars on her arms which she says developed from sores following mosquito bites last year. Also soon after her first ulcer the left leg became numb and began to swell. When first seen by me in the summer, her left leg was cold, with no sensation to pain or touch up to the knee. She is unable to move any part of the leg below the knee. The knee reflex (patellar) is normal. The trophic ulcer now is constantly increasing in size. In the early part of September she developed severe stomatitis with patchy, reddened areas covered with a grayish exudate. Smears were negative for Vincent's organism. The gums also became involved and are much swollen and bleed easily. The condition has remained the same since with but little improvement. A spinal tap done in September revealed a normal cell count, no increase in pressure, normal globulin and sugar, normal colloidal gold and no xanthochromia. The red blood cells number 3,470,000, hemoglobin 65 per cent, white blood cells 13,800, polymorphonuclear cells 82 per cent, lymphocytes 16 per cent, metamyelocytes 2 per cent. She has headaches in the back of the head three or four times a day. The x-ray examinations of the chest and the bones of the leg are negative except for density due to disuse. Pulsation above the ankle is not felt, the foot being swollen. No external pain sensation is present, although there is some deep sensation when exploring the ulcer crater. There is no sensation to hot or cold water. The patient suffers from constipation. The menstrual periods vary from six weeks to six months apart, are scanty, and usually last only one to two days. The blood pressure is 132/80, the urine normal, the Wassermann reaction negative; agglutinations for typhoid, undulant fever and tularemia are negative. Possible syringomyelia or vitamin deficiency are considered. The patient has been given vitamin B complex, nicotinamide, ascorbic acid, liver extract, ferrated liver and the like at one time or another, contrast baths and other treatments, but so far none have done any good.

Carl Baumgartner, M.D., Bismarck, N. D.

ANSWER.—Any attempt to explain this condition on the basis of the facts set forth encounters obstacles somewhere. First, a central nervous system lesion such as syringomyelia is not often found in the lower extremities alone and almost never is so sharply defined. In addition the tactile sense is usually retained. The correspondent does not tell of the neurologic findings elsewhere, so it is assumed that they are normal except for the left leg. A spinal cord tumor or a myelitis would produce changes on both sides.

Secondly, although no pulse may be made out in the lower left leg, it is unlikely that the condition is primarily one of arterial disease. Primary arterial disease is usually associated with pain. Early, before the onset of gangrene, pain is the principal symptom and may be severe. Edema is not a part of arterial disease.

There is obviously a circulatory disturbance. The history of onset with trauma would suggest the occurrence of a thrombophlebitis at the point of injury. It must then be assumed that the process is slowly ascending in the veins of the left leg. At the time the condition was described it must be assumed that the circulation was severely impaired in most of the leg below the knee.

The objection to this hypothesis is that it does not explain the anesthesia in the leg, and it totally disregards the aphthae and the bleeding gums. It is extremely difficult to connect the mouth condition with the disturbance in the leg in the presence of all the other negative findings. It seems unlikely that the situation represents an avitaminosis in view of the lack of response to vigorous vitamin therapy.

To obtain further information it would be well to have a thoroughgoing neurologic examination if this has not already been done. A microscopic examination of a bit of muscle might reveal the presence of some systemic vascular disease. The adequacy of the circulation in the left leg should be investigated with the histamine flare or by careful observation of the skin temperature. Meanwhile the leg should be treated for thrombophlebitis with rest, elevation and perhaps compression. The use of heparin, dicumarol or both should be seriously considered.

PHENYTOIN SODIUM FOR ASTHMA

To the Editor:—Will you please comment on the value of phenytoin sodium in the treatment of bronchial asthma? M.D., Massachusetts.

ANSWER.—Phenytoin sodium (sodium diphenyl hydantoinate, commercially known as Dilantin Sodium) was described in 1937 and 1938 by Merritt and Putnam as a new anticonvulsant. They reported that the drug gave excellent results in the treatment of epilepsy. When large doses were used, toxic effects occurred: nausea and vomiting, nervousness, tremor of the hands, drowsiness, headache, ataxia, hypertrophy of the gums and toxic dermatitis varying from an erythema to a severe morbilliform rash. Patients who received 0.3 Gm. or less daily showed few or no toxic symptoms.

Shulman has reported excellent results in the treatment of 7 asthmatic children. All had severe refractive asthma, with positive cutaneous tests but with indifferent therapeutic results despite the fact that they had been under treatment for at least a year. Phenytoin sodium was given for periods varying from five to twelve months and all other medication was stopped. The initial dosage was ½ grain (0.032 Gm.) twice daily; if symptoms persisted the dosage was increased to ½ grain three times daily, and some patients received as much as 3 grains (0.2 Gm.) a day. Six of the 7 patients were rendered symptom free, although 2 of the children had mild abortive attacks. One patient developed toxic symptoms which cleared rapidly on withdrawal of the drug; this patient was able to resume the treatment with a slightly smaller dose. In 2 cases seasonal nasal and ocular symptoms could not be controlled by the drug. Relief of a concomitant eczema occurred in 2 cases. Shulman notes that, as in epilepsy, the use of phenytoin sodium leads to an improvement in the personalities of some of the children, and he suggests that the drug might be best suited for patients with chronic asthma in whom a psychogenic factor exists. Further studies in this field are necessary, but the results are encouraging.

References:

Putnam, T. J., and Merritt, H. H.: Experimental Determination of the Anticonvulsant Properties of Some Phenyl Derivatives, *Science* **85**: 525 (May 28) 1937.

Merritt, H. H., and Putnam, T. J.: A New Series of Anticonvulsant Drugs Tested by Experiments on Animals, *Arch. Neurol. & Psychiat.* **39**: 1003 (May) 1938.

Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, *The Journal*, Sept. 17, 1938, p. 1068.

Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Seizures: Toxic Symptoms and Their Prevention, *Arch. Neurol. & Psychiat.* **42**: 1053 (Dec.) 1939.

Shulman, M. H.: The Use of Dilantin Sodium in Bronchial Asthma: A Preliminary Report, *New England J. Med.* **226**: 260 (Feb. 12) 1942.

ADMINISTRATION OF MORPHINE

To the Editor:—In the Dec. 19, 1942 issue, page 1349, you published your answer to Major M. Abrams on morphine administration. The remarks on sublingual administration deserve serious reconsideration, as they are based on impressions in the older literature that have not been established. In 1928 this question was studied by actually determining quantitatively the morphine unabsorbed from the sublingual space. It was concluded that little if any was absorbed (Davis, David, and Ayman, David: Sublingual Absorption of Drugs: Morphine, *Arch. Int. Med.* 41: 231 [Feb.] 1928.) It is my impression that the effects of sublingual administration of morphine are those of absorption from the gastrointestinal tract after the drug is swallowed. On the other hand, I fully agree that morphine is quickly and completely absorbed from the gastrointestinal tract. In my experience, when properly administered by mouth, the effects may be as rapid as those following subcutaneous administration. For many years now I have recommended the use of a hypodermic tablet, completely dissolved in an ounce of water, to be followed immediately by a glass or two of water. When the stomach is empty the effects are often experienced within two or three minutes. When given on a full stomach and followed by sufficient water the effects are rapid also. Your statements that the sublingual route protects the morphine from the action of gastric ferments and that morphine is excreted into the stomach are misleading and without foundation (Hatcher, R. A., and Davis, David: The Excretion of Morphine into the Stomach, *J. Pharmacol. & Exper. Therap.* 26: 49 [Aug.] 1925). It is important to inform members of the Medical Corps that morphine is not appreciably absorbed from the mucous membrane of the mouth, as this procedure will undoubtedly delay its action. It is also important to emphasize that morphine may be quickly absorbed from the gastrointestinal tract if taken in complete solution. The method suggested is a hypodermic tablet completely dissolved in water, and then followed by water, to wash it into the circulation. David Davis, M.D., Boston.

EXPRESSIONS OF VISUAL ACUITY

To the Editor:—Ophthalmologists are accustomed to designate their findings on visual acuity by referring to a standard distance (for instance 20/50, 20/80). On the other hand, it seems that in all tests given by the services a standard size letter is used and the examinee has to approach this letter until he is able to read it. Therefore the official designations of visual acuity for the services read 12/20, 15/20 and so on. Examiners may have difficulty in comparing these two different kinds of designations. There is a simple way of conversion, by dividing the figure one wants to convert into 400. For instance:

20/25 of the ophthalmologist's designation equals 16/20 since 400 divided by 25 equals 16

12/20 of the services' designation equals 20/33 since 400 divided by 12 equals 33.

I hope these remarks will be helpful.

Arthur Linksz, M.D., Hanover, N. H.